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13. ABSTRACT *(Maximum 200 words)*

Extending work begun as part of an National Cancer Institute-funded project, we are examining whether variations in care received by older women affect short-term psychosocial and clinical outcomes. Our specific aims are: 1) To describe patterns of adjuvant hormonal and chemotherapy in older women, and factors associated with receipt of these therapies; 2) To characterize and quantify the breast cancer-related care received by older women during the early years following diagnosis; and 3) To determine the effects of ongoing breast cancer care on patients' quality of life. We are conducting a longitudinal observational study of a cohort of 303 women ≥ 55 years of age diagnosed with stage I and II breast cancer between October 1992 and December 1995 at five sites in Boston, Massachusetts. Women are interviewed annually to obtain information about health and personal characteristics. Medical record abstracts are performed annually to gather information about treatments received, tests performed, and disease recurrences. We will identify patient and provider characteristics associated with variations in care received and the effects of these variations on patients' quality of life.

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Rebecca A. Sullivan 8/6/99

PI - Signature Date

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5. INTRODUCTION

Little is known about what constitutes appropriate care for older women with breast cancer (1) because until recently, women ≥ 70 years of age were excluded from most clinical trials. It is perhaps not surprising, therefore, that there is considerable variation in how older women are treated (2-9). The current study is designed to identify determinants of variations in adjuvant hormonal/chemotherapy and follow-up care among older women with early stage breast cancer and the effects of these variations on health-related quality of life and breast cancer-specific function. As described in more detail below (**6. BODY**), we are studying a cohort of women ≥ 55 years of age with newly diagnosed early stage breast cancer over a 4 year time period. Initial telephone interviews are conducted at 3-5 months following initial definitive treatment, with subsequent interviews occurring approximately two years later, and annually thereafter for two years. Medical records are abstracted, beginning at the time of diagnosis and continuing until project completion, or the development of metastatic disease or subject death. The medical record review covering the initial treatment period and the baseline interview were funded by the National Cancer Institute. The follow-up interviews and medical record reviews are funded under the current project by the US Army Medical Research, Development, Acquisition and Logistics Command.

We are filling important gaps in knowledge by addressing the following **study questions** in our current study:

1. What patient and provider characteristics are associated with the receipt of hormonal and/or chemotherapy?
2. What are the effects of hormonal treatment on patients' quality of life?
3. What patient and provider characteristics are associated with the receipt of surveillance tests?
4. What are the effects of surveillance testing on patients' quality of life?

6. BODY

<u>Overview and Findings from the Parent Study Funded by the National Cancer Institute (CA57754)</u>

Funding from the National Cancer Institute (NCI) enabled us to enroll the cohort that is being followed longitudinally for the current project. Patients ≥ 55 years of age with newly diagnosed early stage breast cancer, being cared for at one of five hospitals with academic affiliation in Boston, Massachusetts, were enrolled between January 1993 and April 1996. Eligible patients were sent an introductory letter signed by their surgeon and a consent form approximately three months following initial surgical treatment. This was followed by a telephone call from our interviewer who further explained the study, answered questions, and obtained informed consent. Data were collected via a review of patients' surgical records, and a 30 minute computer-assisted telephone interview with consenting eligible patients. Data collected from medical records included: histology, stage, estrogen receptor status, surgery performed, additional therapies received, and medical comorbidities. Our patient telephone interview included questions about: general health-related quality of life, breast cancer-specific

quality of life, medical comorbidities, the treatment decision-making process, treatment priorities, perceptions of doctor-patient communication, and demographic characteristics.

Included with our 1998 report were two papers in published in 1997 and 1998 (10, 11) in ***Cancer*** that summarize the methods and findings from the baseline data. Two related papers, but whose topics were not central to the specific aims of the original grant, were published in early 1999 (12, 13).

The first addresses upper-body function following primary tumor therapy:

RISK FACTORS FOR A DECLINE IN UPPER BODY FUNCTION FOLLOWING TREATMENT FOR EARLY STAGE BREAST CANCER (see Appendix for reprint)

Abstract
Purpose: To identify risk factors for a decline in upper body function following treatment for early stage breast cancer.
Methods: We conducted a cross-sectional observational study of 213 women ≥ 55 years of age newly diagnosed with early stage breast cancer interviewed three to five months following their definitive surgery. Patients were classified as having impaired upper body function related to their breast cancer treatment if: 1) they reported having no difficulty in performing any of three tasks requiring upper body function (pushing or pulling large objects; lifting objects weighing more than 10 pounds; and reaching or extending arms above shoulder level) prior to treatment, but reported that any of these tasks were *somewhat* or *very* difficult in the four weeks prior to interview, or 2) they reported that performing any of the three tasks requiring upper body function was *somewhat* difficult prior to treatment, but reported that any of these tasks were *very* difficult in the four weeks prior to interview.
Results: In multiple logistic regression models, both the extent and type of primary tumor therapy and cardiopulmonary comorbidity were significantly associated with a decline in upper body function following breast cancer treatment.
Conclusion: Given the critical importance of upper body function in maintaining independent living, clinicians should consider the functional consequences of treatment when they discuss treatment options and post-operative care with older women who have early stage breast cancer.

The second is a methodological paper that compares different strategies for measuring comorbidity:

COMPARISON OF INTERVIEW-BASED AND MEDICAL RECORD-BASED INDICES OF COMORBIDITY AMONG BREAST CANCER PATIENTS (see Appendix for reprint)

Abstract
Objectives: To compare patient interview-based and medical record-based measures of comorbidity and their relation to a range of patient outcomes, including primary tumor therapy and mortality, self-reported upper body function, and overall physical function.
Methods: 303 breast cancer patients age 55 years or older and diagnosed at 1 of 5 Boston hospitals were enrolled. Patient interviews and medical record abstracts provided the information necessary to construct the Charlson index, Satariano index, and a new interview-

based index of cardiopulmonary comorbidity. These indices were used alone and in combination to predict the patient outcomes.
Results: The indices of comorbidity corresponded well with one another. The record-based Charlson index was the only index that predicted receipt of definitive therapy. No index of comorbidity predicted mortality over the short follow-up period. The new interview-based index of cardiopulmonary comorbidity was a better predictor of upper-body function and overall physical function than the interview-based or medical record-based Charlson or Satariano indices of comorbidity.
Conclusion: Older breast cancer patients are able to provide information about their diseases and related symptoms that correlates well with medical record-based measures of comorbidity and displays similar patterns of predictive power. A new self-reported measure of cardiopulmonary comorbidity performs better than the medical record-based measures for predicting patient-related functional outcomes.

Experimental Methods Used for Current Study

Institutional Review Board Approval: All annual Institutional Review Board approvals were obtained from each of the study sites. We received approval from Faulkner Hospital on November 14, 1995; from Boston Medical Center on November 15, 1995; from Boston City Hospital on December 27, 1995; from Beth Israel Hospital on October 16, 1995; and from New England Medical Center on December 12, 1995. Approvals are updated annually.

Study Implementation (Summary of Progress with Tasks 1-4, STATEMENT OF WORK, Revised February 1999)

Subject Enrollment and First Follow-up Interview in the Current Study. Subjects enrolled in the NCI study were mailed a consent packet 20 months after their diagnosis date. This time interval was chosen because it was the shortest interval from initial diagnosis possible with the initiation of the US Army Research, Development, Acquisition and Logistics Command funding.

It should be noted that the sample size available for study and the sample characteristics were constrained by the design and implementation of the parent NCI study. Specifically, although enrollment for the parent study was extended until April 1996, we did not achieve the sample size of 350 that we had originally planned (the reasons for this were detailed in the 1997 report). In addition, the original study was designed to compare younger postmenopausal women with older postmenopausal women. Two factors resulted in the youngest group of women (55-64 years of age) being the greatest contributors to our sample, and the oldest group of women (75+) being the smallest contributor. First, the number of women 55-64 years of age at risk for breast cancer is far greater than the number of women 75+ years of age at risk. Second, we, like all other investigators, experienced the highest refusal rate among the oldest group of women.

As noted in our 1998 report, we completed data collection for the first follow-up interview in 1998. Of the 303 subjects who were eligible, 250 (83%) participated in this first follow-up interview. The reasons for non-participation included: 1) inability to contact – 30 (10%), 2) refusal – 16 (5%), 3) death – 5 (2%), and 4) too ill – 2 (1%).

Second Follow-up Interview. Our second follow-up interview occurs approximately 12 months after the first follow-up interview. Data collection for this interview was completed in 1999. A total of 225 subjects completed their second follow-up interview. This number reflects 215 subjects who participated in the baseline and first follow-up interviews and 10 who completed baseline interviews but could not be located for their first follow-up interviews. Of those who were eligible but not interviewed, 11 refused (this includes 6 who could not be located for their first follow-up interview but who, when located for their second follow-up interview, refused participation); 10 had died, 2 were too sick, and 24 who were unable to be located (this includes 5 who could not be located for their first follow-up interview either).

Third Follow-up Interview. Our third follow-up interview occurs approximately 12 months after the second follow-up interview. To date, 177 subjects have completed their third and final follow-up interview. This includes 3 subjects who did not complete their second follow-up interview. A total of 42 (20%) have not participated. Twenty-six could not be reached because residence and/or telephone numbers had changed. Eleven had died and 2 were too ill to participate. Three (1 %) refused to participate. All third follow-up interviews will be completed by December 31, 1999.

Collection of Surveillance Data. Medical record abstractions began in November 1994, and additional medical record abstractions are performed annually for each participant. To assess inter-rater reliability, a 20% random sample of charts are reviewed by Dr. Silliman. Medical record abstractions have been completed for subjects who have completed the first follow-up interview. We were able complete 247 of 250 abstractions (99%). Two records were inaccessible because the patients had died and one patient received no further treatment or care. Abstractions have been completed for 208 of the 225 (92%) of subjects who completed the second follow-up interview. Four records were inaccessible because the patients had died; four patients received no further treatment; five records could not be accessed because our original consent forms were considered to be out of date; and four records could not be located. Of the 177 subjects who have completed the third follow-up interview, abstractions have been completed for 118 (67%). All abstractions will be completed by December 31, 1999.

Results for Current Study (Summary of Progress with Tasks 5-6, STATEMENT OF WORK, Revised February 1999)

Study Question #1. What patient and provider characteristics are associated with the receipt of hormonal and/or chemotherapy?

Based on reviewers' comments about our manuscript addressing primary tumor therapy ("The Impact of Age, Marital Status, and Physician-Patient Interactions on the Care of Older Women with Breast Cancer"), we chose to address this question by analyzing the outcome according to the receipt of both primary tumor therapy as well as adjuvant systemic therapy. Thus, patients could be classified as yes/yes, yes/no, no/yes, and no/no. The manuscript has been accepted for publication in *Medical Care* and will be published in October 1999 (14).

THE CARE OF OLDER WOMEN WITH EARLY STAGE BREAST CANCER: WHAT IS THE ROLE OF SURGEON GENDER? (See Appendix for the manuscript)

Abstract

Background. - Over the past decade and a half a substantial literature has documented age-dependent variations in breast cancer care. Accumulating evidence suggests that these variations do impact the health outcomes of older women with breast cancer. Surgeon gender may be an important source of age-dependent variations in care.

Objective. - To examine the relationship between surgeon gender and primary tumor therapy and systemic adjuvant therapy among 303 older women with early stage breast cancer cared for by 20 surgeons in Boston, Massachusetts.

Research Design. - Cross-sectional observational study.

Subjects. - Women at least 55 years of age with newly diagnosed stage I or II breast cancer.

Main Outcome Measure. - Definitive primary tumor therapy and systemic adjuvant therapy.

Results. - After adjustment for patient and tumor characteristics, patients of female surgeons were more likely to receive definitive treatment, with the strongest effect being observed for the receipt of both definitive primary tumor therapy and systemic adjuvant therapy (OR 4.5; 95% CI 2.7, 7.7).

Conclusions. - Women with early stage breast cancer cared for by female surgeons are more likely to receive standard therapies. Surgeons provide the initial care for all women with breast cancer – both diagnostic as well as therapeutic care. Their role in breast cancer care is pivotal and has a substantial impact on the nature of breast cancer care received.

Study Question #2. What are the effects of hormonal treatment on patients' quality of life? **[Unpublished data]**

We have taken advantage of our longitudinal data (baseline, first follow-up interview, and second follow-up interview) to address several questions related to hormonal treatment, including this study question. First, we have examined predictors of taking tamoxifen at any time during this approximately three years of follow-up. After taking into account patients' age, marital status, comorbidity, risk of recurrence, and primary tumor therapy, their educational attainment, and baseline physical function and emotional health are significant predictors of tamoxifen therapy. Women who are more highly educated (OR=2.8, 95% CI 1.1, 7.1) or who had better emotional health at baseline (OR=1.3, 95% CI 1.0, 1.7) were more likely to receive tamoxifen. Women who were more physically functional at baseline were less likely to receive tamoxifen (OR=0.7, 95% CI 0.6, 0.9). Second, we have examined predictors of stopping taking tamoxifen during the three years of follow-up. Again, after taking into account patients' age, marital status, education, cormobidity, number of other medications taken, physical function, and emotional health, their risk of recurrence and primary tumor therapy were significant predictors of stopping tamoxifen. Worries about breast cancer was of marginal significance. Women at low risk of recurrence (OR=0.21, 95% CI 0.04, 1.0) and who had received definitive primary tumor therapy (OR=0.2, 95% CI 0.1, 0.7) were less likely to quit taking tamoxifen; those at high risk of recurrence and who had not received definitive therapy were more likely to quit taking tamoxifen. Women who were more worried about breast cancer and its recurrence were also less likely to quit taking tamoxifen (OR=0.8, 95% CI 0.6, 1.0). These data suggest that there is a group of women who, by virtue of being at high risk of recurrence due to their tumor

characteristics and not having received appropriate primary tumor therapy, are at even greater risk due to the premature stopping of tamoxifen therapy.

The presence or absence of side effects was not associated with stopping tamoxifen therapy. However, we were interested in the characteristics of patients who experience any side effects and more specifically hot flashes, since the latter is the most commonly reported side effect. The reporting of any side effects did not change with duration of therapy. Younger women, women with poorer emotional health at baseline, and women with more breast cancer worries were more likely to report side effects of tamoxifen (all $p < 0.05$), than were older women, those with better baseline emotional health, and those with fewer breast cancer worries. Younger women were also more likely to report more side effects of tamoxifen, even when hot flashes are considered separately. The reporting of hot flashes did decrease with duration of therapy, however. Younger women and those with poorer baseline emotional health were more likely to report hot flashes ($p < 0.001$), than were older women and those with better baseline emotional health.

Analyses examining predictors of changes in quality of life from baseline to the second follow-up interview are in progress. These will be completed when the third follow-up interviews have been completed. Analytic techniques that we apply to this question will inform our approach to Study Questions #3 and #4 below.

Study Question #3. What patient and provider characteristics are associated with the receipt of surveillance tests?
Study Question #4. What are the effects of surveillance testing on patients' quality of life?

In previous reports we have provided preliminary data regarding surveillance testing. Our plan is to address these two very important questions when we have completed our medical record abstracting in December 1999. This information will be included in our final report.

Additional Analyses

In addition to addressing Study Question #2 above by taking advantage of the longitudinal nature of our data, we have examined the relationship between patient characteristics and treatments and a decline in upper body function over the first two years of follow-up. This manuscript has been submitted for publication:

PATIENT CHARACTERISTICS AND TREATMENTS ASSOCIATED WITH A DECLINE IN UPPER-BODY FUNCTION FOLLOWING BREAST CANCER THERAPY (see Appendix for the manuscript)

Abstract
Breast cancer therapy is often followed by a decline in upper-body function. 303 women diagnosed with Stage I or II breast cancer were interviewed 5 and 21 months after surgery and their medical records were reviewed. Women with cardiopulmonary comorbidity had an odds ratio for decline at the 5 month interview of 2.8 (95 percent CI 1.3-5.7), relative to women without. Women who received mastectomy (OR = 2.5; 95 percent CI 0.9-6.7) or breast conserving surgery with radiation therapy (OR = 2.9; 95 percent CI 1.0-8.9) were at higher risk for decline at the 5 month interview than women who received only breast conserving surgery.

Women who had axillary dissection were more likely to report numbness or pain in the axilla (OR = 6.4; 95 percent CI 1.2-33) at the 21 month interview than women who did not. Clinicians should consider the functional consequences of treatment when discussing treatment options and post-operative care with women who have early stage breast cancer.

Recurrence and Mortality

We will also be examining breast cancer recurrence and mortality in relation to primary tumor therapy and systemic adjuvant therapy. Recurrence information is provided by our annual medical record surveillance abstractions. In addition, we obtain information regarding deaths from physicians, families, and local newspaper obituaries. As of this writing, twenty-six subjects have died (9%). We have obtained death certificates for 23 of these from the Massachusetts Department of Vital Records. Fifteen (65%) died of breast cancer and 8 (35%) died of other causes. To more comprehensively obtain information on patient deaths we submitted an application to the US Department of Health and Human Services in May 1999 for use of the National Death Index (NDI). On July 22, 1999 we received notification that our application was approved. Because of the time lag in updating of information in the NDI (1998 data will not be available until January 2000), the time period to be covered will be 1993-1998.

Plans for the 06 Project Year

We have been granted a two year extension of the project so that we can obtain complete follow-up for all consenting subjects that we can reach. During the 06 Project Year (final 9 months of the proejct) we will complete all Follow-up 3 interviews and all medical record surveillance abstractions. Final analyses related to surveillance testing will be completed during this final year and a manuscript describing findings in relation to hormonal therapy will be prepared.

7. KEY RESEARCH ACCOMPLISHMENTS

• Successful completion of all aspects of the project excepting the completion of the third and final follow-up interviews, the final year of medical record surveillance, and final analyses.

• See **8. REPORTABLE OUTCOMES** below.

8. REPORTABLE OUTCOMES

Manuscripts, Abstracts, and Presentations

a. Dr. Silliman was invited to write an editorial as a companion to an article on age-related treatment variations published in the Journal of the National Cancer Institute June 4, 1996. Silliman RA. Breast cancer care in older age: Where do we go from here?

b. Five research reports have been published, or are *in press.*

1) Silliman RA, Troyan SL, Guadagnoli E, Kaplan SH, Greenfield S. The impact of age, marital status, and physician-patient interactions on the care of older women with breast cancer. Cancer 1997; 80:1326-34.
2) Silliman RA, Dukes KA, Sullivan LM, Kaplan SH. Breast cancer care in older women: Sources of information, social support, and emotional health outcomes. Cancer 1998; 81:706-11.

3) Silliman RA, Prout MN, Field T, Kalish SC, Colton T. Risk factors for a decline in upper body function following therapy for early stage breast cancer. Breast Cancer Research and Treatment 1999;54:25-30.

4) Silliman RA, Lash TL. Comparison of interview-based and medical record-based indices of comorbidity among breast cancer patients. Med Care 1999;37:339-49.

5) Silliman RA, Demissie S, Troyan SL. The care of older women with early stage breast cancer: What is the role of surgeon gender? Med Care 1999;37:*in press.*

c. Another manuscript has been submitted for publication:

Lash TL, Silliman RA. Patient characteristics and treatments associated with a decline in upper body function following breast cancer therapy.

d. Dr. Silliman has co-authored three book chapters with Dr. Lodovico Balducci:

1) Balducci L, Silliman RA, Baekey P. Breast cancer: An oncological perspective - Part I. In: Balducci L, Lyman GH, Ershler WB, eds. Comprehensive Geriatric Oncology. Australia:Harwood Academic Publishers, 1998:629-660.

2) Silliman RA, Balducci L. Breast cancer: A geriatric perspective - Part II. In: Balducci L, Lyman GH, Ershler WB, eds. Comprehensive Geriatric Oncology. Australia:Harwood Academic Publishers, 1998:661-664.

3) Silliman RA, Balducci L. Breast cancer. In: Gallo JJ, Busby-Whitehead J, Rabins PV, Silliman RA, Murphy JB, eds. Reichel's Care of the Elderly: Clinical Aspects of Aging (5th ed). Baltimore: Williams & Wilkins, 1999:407-413.

e. Dr. Silliman was invited to speak at the Cancer in the Elderly 1996 Conference (November 1996), at a lecture series sponsored by the Massachusetts Department of Health (January 1997), at a special meeting of medical oncology educators in Puerto Rico (February 1997), and at a conference convened by the National Institute on Aging and the National Cancer Institute to address comorbidity measurement in older cancer patients (July 1999).

f. Dr. Silliman was invited to participate in a two and one-half day retreat to assist the National Cancer Institute's Breast Cancer Progress Review Group (September 1997) in developing a breast cancer research agenda for the next five years.

Funding Applied for Based on Work Supported by this Award

Dr. Silliman (Principal Investigator) and colleagues submitted a grant proposal to the National Cancer Institute June 1, 1995 entitled "Adjuvant Tamoxifen Therapy in Old Age: Determinants and Consequences" (R01 CA/AG 70818). It was funded and began September 30, 1996. The current project is much smaller in scope but provided important preliminary data for the new project. This new project is examining patterns of adjuvant tamoxifen prescribing patterns in much more detail and is enrolling patients ≥ 65 years of age at four sites (Los Angeles, Minnesota, Rhode Island, and North Carolina). About 750 women have consented to participate thus far and the target enrollment figure is 900. About half are ≥ 75 years of age. A follow-up proposal entitled "Breast Cancer Treatment Outcomes in Older Women" (RO1 CA84506) was submitted February 1, 1999. Again, the current project provided important preliminary data. A funding decision is pending at this time.

9. CONCLUSIONS

Because the current project is as yet not complete, we cannot comment regarding project implications.

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14. Silliman RA, Demissie S, Troyan SL. The care of older women with early stage breast cancer: What is the role of surgeon gender? Med Care 1999;37:*in press*.

11. APPENDIX

Breast Cancer Research and Treatment **54:** 25–30, 1999.

Report

Risk factors for a decline in upper body function following treatment for early stage breast cancer

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Key words: breast cancer treatment, older women, upper body function

Summary

Purpose: To identify risk factors for a decline in upper body function following treatment for early stage breast cancer.

Methods: We conducted a cross-sectional observational study of 213 women $\geq$ 55 years of age newly diagnosed with early stage breast cancer interviewed three to five months following their definitive surgery. Patients were classified as having impaired upper body function related to their breast cancer treatment if: 1) they reported having no difficulty in performing any of three tasks requiring upper body function (pushing or pulling large objects; lifting objects weighing more than 10 pounds; and reaching or extending arms above shoulder level) prior to treatment, but reported that any of these tasks were somewhat or very difficult in the four weeks prior to interview, or 2) they reported that performing any of the three tasks requiring upper body function was somewhat difficult prior to treatment, but reported that any of these tasks were very difficult in the four weeks prior to interview.

Results: In multiple logistic regression models, both the extent and type of primary tumor therapy and cardiopulmonary comorbidity were significantly associated with a decline in upper body function following breast cancer treatment.

Conclusion: Given the critical importance of upper body function in maintaining independent living, clinicians should consider the functional consequences of treatment when they discuss treatment options and post-operative care with older women who have early stage breast cancer.

Introduction

Breast cancer has become increasingly common among older women. The incidence of breast cancer increases with age until at least the ninth decade of life, the number of older women at risk has increased, and the age-adjusted incidence has increased, in part due to increased use of screening mammography [1]. Furthermore, the increasing use of screening mammography has resulted in a greater proportion of older women being diagnosed with early stage disease [2]. Earlier diagnosis, coupled with an overall increase in longevity in late life, will likely result in an increase in the number of older women who are long-term survivors of breast cancer. For these women, the functional consequences of breast cancer treatment, manifested in tasks that require upper body strength, are likely to assume greater importance, particularly as they concomitantly acquire age-related disabilities.

Satariano and colleagues studied the functional consequences of breast cancer therapy and found that among women aged 55–74 who were treated for breast cancer, at three months following diagnosis they were more likely than controls without breast cancer to report difficulty in completing tasks that required upper body strength [3]. In another study by the same investigative team, analyses conducted with the case group failed to find a treatment effect. However, the treatment measure categorized radiation, chemotherapy, and hormonal therapy together as 'adjuvant therapy'. Thus, it was not possible to evaluate the effects of standard therapies or of the

specific components of these therapies on upper body function [4].

Because tasks that require upper body strength are crucial for maintaining independence, it is important to identify risk factors for breast cancer patients' decline in abilities to perform such tasks. Knowledge of these risk factors may aid in the identification of women at high risk for poor functional outcomes and in the choice of their primary breast cancer treatment.

We therefore conducted a cross-sectional study of women $\geq$ 55 years of age at three to five months after their treatment for newly diagnosed stage I and stage II breast cancer to identify risk factors for a decline in upper body functional abilities in relation to treatments received.

Methods

Sampling

Details of the study have been descibed elsewhere [5]. In brief, we studied women $\geq$ 55 years of age, newly diagnosed with histologically confirmed stage I and stage II invasive breast carcinoma cared for at one of five hospitals in Boston, Massachusetts. Potential study participants were sent an introductory letter signed by their surgeon and a consent form at approximately two to three months following their definitive surgical treatment. An interviewer followed-up with a telephone call to explain the study further, to answer questions, and to obtain informed consent. We restricted the analyses described herein to those women interviewed three to five months following their definitive surgery to minimize variation associated with differing length of recovery time.

Data collection

Data were collected via a review of patients' surgical records and a 35 min computer-assisted telephone interview with consenting eligible patients. Data collected from medical records included: tumor size, axillary node status, breast surgery or surgeries performed (mastectomy or breast conserving surgery, with or without axillary dissection), and whether or not the patient received a course of post-operative radiation therapy. The patient telephone interview included questions about tasks that required upper body function and were asked in relation to breast cancer treatment:

1. pushing or pulling large objects, such as a living room chair,
2. lifting objects weighing more than 10 pounds, such as a heavy bag of groceries, and
3. reaching or extending arms above shoulder level.

For each task, the subject was asked about its difficulty (very, somewhat, or not difficult) in performance during four weeks preceding interview as well as prior to their breast cancer treatment. These items were selected from the items used by Satariano and colleagues [3], fielded previously in the Framingham Disability Study [6] and derived from the original work of Nagi [7]. In addition, we asked questions about cardiopulmonary comorbidities that were part of the Total Illness Burden Index [8], as well as about demographic characteristics (age, race, marital status, education, height, and weight).

Major analytic variables

Our dependent variable was a decline in upper body function in relation to breast cancer treatment. Patients were classified as having a decline in upper body function in relation to their breast cancer treatment if:

1. they reported having no difficulty in performing any of the three tasks requiring upper body function prior to treatment, but reported that any of these tasks were somewhat or very difficult in the four weeks prior to interview, or
2. they reported that performing any of the three tasks requiring upper body function was somewhat difficult prior to treatment, but reported that any of these tasks were very difficult in the past four weeks.

For our independent variables we considered: age (55–64, 65–74, 75+ years) and education (< high school/ $\geq$ high school). We also considered body mass index (BMI: weight in kilograms divided by height in meters squared); comorbidity (a continuous measure based on patients' reports of diagnoses of chronic obstructive pulmonary disease, congestive heart failure, and ischemic heart disease and related symptoms, with a positive score reflecting above average comorbidity); breast cancer characteristics, including tumor size ($\leq$1 cm, >1–2 cm, >2 cm) and node status (positive/negative); and breast cancer treatments received. For the breast cancer treatments variables, we used two different approaches. First, we considered each of the two standard treatments (modified radical mastectomy and breast conserving surgery with axillary dissection followed by radiation therapy) in comparison to other primary therapies received (e.g. breast conserving surgery without radiation therapy). Second, we considered the specific components of primary tumor

therapy (axillary dissection, definitive surgery [mastectomy vs. breast conserving surgery], and radiation therapy).

Analytic strategy

We obtained descriptive statistics for all study variables. We then performed a series of bivariate analyses, examining the relationships between independent variables and the dependent variable, using independent samples t-tests and Chi-square tests as appropriate. Next, we developed multiple logistic regression models whose independent variables included all the statistically significant associations ($p < 0.05$) found in bivariate analyses, as well as all breast cancer treatment variables. We used stepwise multiple logistic regression techniques with significance criterion of 0.1 for entry or removal from the model.

Results

Two hundred thirteen women (71%) from the original cohort were interviewed three to five months following their definitive surgery and served as the study sample for this analysis. Sample characteristics are similar to those of the full cohort [5]. Almost two-thirds (59%) were $\geq$ 65 years of age. Most were white (95%) and had a high school education or greater (84%). Half were married; most of the remainder were widowed. The average BMI was 25.98 ($\pm$5.05) and the average comorbidity score was 1.48 (range 0–15). Most patients had small tumors (77% $\leq$ 2 cm) and were node negative (80%). The majority (57%) had undergone breast conserving surgery with axillary dissection followed by radiation therapy; 23% had undergone modified radical mastectomy. Of the 43 who received other than these standard primary tumor therapies, 23 underwent breast conserving surgery followed by radiation but without axillary dissection; 12 underwent breast conserving surgery and axillary dissection but did not receive radiation therapy; five underwent breast conserving surgery but neither axillary dissection nor radiation therapy; and the remainder either underwent simple mastectomy without radiation ($n = 2$) or underwent biopsy or radiation therapy only ($n = 2$). About a third of all subjects (35%) reported a decline in upper body function following their breast cancer treatment.

On bivariate analysis (Table 1), women who reported a decline in upper body function since breast cancer treatment had higher BMIs and cardiopulmonary comorbidity scores than those who did not report worsened upper body function. In addition, women who received other than standard primary tumor therapies were less likely to report worsened upper body function than those who received either breast conserving surgery with axillary dissection and radiation therapy or a modified radical mastectomy (23% vs. 36% and 42%, $p = 0.15$). With respect to the individual components of primary tumor therapy, women who underwent axillary dissection, mastectomy, or radiation therapy were all somewhat more likely to report a decline in upper body function since treatment than those who did not, but none of these relationships reached statistical significance.

In a multiple logistic regression model that included standard therapies (modified radical mastectomy and breast conserving surgery with axillary dissection followed by radiation therapy), with non-standard primary tumor therapies as the referent group (Table 2, Model 1), women who received breast conserving surgery with axillary dissection and follow-up radiation therapy were 2.2 times more likely to report a decline in upper body function ($p = 0.08$), and women who received modified radical mastectomy were 2.8 times more likely to experience a decline in upper body function ($p = 0.04$). Cardiopulmonary comorbidity was also an independent predictor of a decline in upper body function ($p = 0.002$). In a second multiple logistic regression model (Table 2, Model 2), women undergoing mastectomy or radiation therapy were each more than six times more likely to report a decline in upper body function than those who did not ($p = 0.01$). As in Model 1, cardiopulmonary comorbidity also was an independent predictor of a decline in upper body function following breast cancer treatment ($p = 0.006$).

Discussion

We have found that among older women with early stage breast cancer, the extent of primary tumor therapy, as well as specific components of therapy, and self-reported cardiopulmonary comorbidity are risk factors for a decline in upper body function during the early months following primary breast cancer therapy. To our knowledge, this is the first study to evaluate both the early effects of different treatment regimens as well as comorbidity in a group of older women with early stage breast cancer.

Sneeuw and colleagues examined late functional outcomes (an average of four years after treatment) among women of various ages who received breast conserving surgery, axillary dissection, and radiation therapy. In this study from the Netherlands of 76 women (age range 37–75) who were treated between

Table 1. Bivariate relationships between patient characteristics and decline in upper body function ($n = 213$)

Characteristic	Declined ($n = 74$)	Not declined ($n = 139$)	p Value
Demographic characteristics			
Age (n, %)			
55–64	30 (34)	58 (66)	0.97
65–74	30 (36)	54 (64)	
75+	14 (34)	27 (66)	
Education (n, %)			
< High school	14 (40)	21 (60)	0.50
≥ High school	60 (34)	116 (66)	
General health status (mean, SEM)			
Body mass index (BMI)	26.95 (0.67)	25.45 (0.40)	0.054
Comorbidity	2.27 (0.41)	1.07 (0.17)	0.009
Breast cancer characteristics			
Tumor size (n, %)			
≤1 cm	19 (32)	41 (68)	0.76
>1–2 cm	33 (36)	59 (64)	
>2 cm	18 (38)	29 (62)	
Node status (n, %)			
Negative	57 (34)	113 (66)	0.58
Positive	16 (38)	26 (62)	
Breast cancer treatments			
Primary tumor therapy (n, %)			
Modified radical mastectomy	22 (42)	31 (58)	0.15
Breast conserving surgery/ axillary dissection/radiation therapy	43 (36)	77 (64)	
Other	9 (23)	31 (77)	
Specific treatment modalities (n, %)			
Axillary dissection			
Yes	65 (36)	117 (64)	0.33
No	8 (27)	22 (73)	
Mastectomy			
Yes	22 (42)	31 (58)	0.23
No	52 (33)	108 (67)	
Radiation therapy			
Yes	54 (37)	93 (63)	0.36
No	20 (30)	46 (70)	

1975 and 1985, nearly half of the subjects reported a little (34%) or moderate (13%) limitation of movement in the arm and shoulder on the treatment side [9]. Gerber and colleagues compared functional outcomes among participants in a randomized clinical trial who received either modified radical mastectomy or breast conserving surgery with axillary dissection and follow-up radiation therapy. All subjects also participated in an extensive structured rehabilitation program. The average number of days to reach functional range of motion did not differ between the groups, but twice as many women who were treated in the breast conserving surgery treatment group reported chest wall tenderness one year after treatment, as compared to the women in the modified radical mastectomy treatment arm (58.4% vs. 27.4%, $p < 0.0001$) [10]. These data suggest that

Table 2. Multiple logistic regression models predicting a decline in upper body function in relation to breast cancer treatment

Characteristics	β coefficient	Odds ratio (95% CI)
Model 1		
Primary tumor therapy		
Other (referent)	–	–
Breast conserving surgery	0.7863	2.20 (0.92, 5.23)
Modified radical mastectomy	1.0322	2.81 (1.08, 7.32)
Cardiopulmonary comorbidity	0.1721	1.19 (1.06, 1.33)
Model 2		
Mastectomy	2.0377	7.67 (1.66, 35.55)
Radiation therapy	1.8826	6.57 (1.45, 29.87)
Cardiopulmonary comorbidity	0.1560	1.17 (1.05, 1.31)

breast conserving surgery in conjunction with axillary dissection and radiation therapy may have substantial late functional consequences.

Our data are consistent with these investigations and extend those of Satariano and colleagues [3, 4]. They demonstrate that there are early functional consequences among older women who receive either modified radical mastectomy or breast conserving surgery with axillary dissection followed by radiation therapy, although the risk associated with modified radical mastectomy is greater. Furthermore, our treatment component-specific analyses suggest that radiation therapy contributes to the increased risk of functional decline among women who undergo breast conserving surgery, in keeping with the findings of Gerber and colleagues [10]. In our data, axillary dissection does not appear to have an independent influence, once the effects of type of surgery and radiation are taken into account. This may be because our measure of upper body function was insensitive to the difficulties experienced by women who undergo axillary dissection, or because the number of women who did not receive axillary dissection was relatively small. The advent of lymphatic mapping and sentinal lymph node biospy may decrease substantially the need for axillary dissection in the not distant future [11].

Finally, cardiopulmonary comorbidity burden also is a risk factor for a decline in upper body function following primary tumor therapy. Tasks that require upper body strength stress the cardiopulmonary system. Thus, cardiopulmonary disease burden may limit rehabilitation efforts during the early treatment recovery period.

Of interest, the group of women at least risk for a decline in upper body function, were those who received less than standard primary tumor therapy. It is therefore important to consider whether the offering of less intensive treatment may preserve upper body function at the expense of longer term survival. A recent study by Goodwin and colleagues has documented that older women who receive less than standard breast cancer therapy are at greater risk of dying from their breast cancer than those who receive standard therapy [12]. Furthermore, recent breast cancer mortality trends document that breast cancer mortality has decreased in all age groups except the oldest old, who are also at greatest risk for receiving less than standard treatment [2]. For many older women, the better short-term functional status associated with less intensive treatment may not offset the increased risk of breast cancer mortality.

Our findings must be considered with the study's major limitations in mind. First, we did not measure directly upper body function, either before or after treatment. Second, we did not gather side-specific information, either in relation to handedness or the side on which treatments were performed. Third, we did not collect information about prior recreational or occupational injuries involving the upper extremities. Fourth, our sample was relatively small and the confidence intervals around our estimates of risk are wide. Nonetheless, our data are consistent with the limited number of studies to date and make clinical sense. Whether the early impairments that we have observed will persist awaits the collection of follow-up data.

Given the critical importance of upper body function in maintaining independent living [13], our findings suggest that clinicians should consider the functional consequences of treatment when discussing treatment options and post-operative care with older women who have early stage breast cancer. For example, women who have cardiopulmonary comorbidity, regardless of the primary therapy that they chose,

are likely to benefit from a supervised rehabilitation program. In addition, women who undergo both modified radical mastectomy and radiation therapy may be another group most likely to benefit from such a program. Finally, we need to design studies to find the best balance between treatment efficacy and functional morbidity for this group of patients.

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Comparison of Interview-Based and Medical-Record Based Indices of Comorbidity Among Breast Cancer Patients

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OBJECTIVES. To compare patient interview-based and medical-record based measures of comorbidity and their relation to primary tumor therapy, all cause mortality, self-reported upper body function, and overall physical function.

METHODS. Three-hundred and three breast cancer patients (≥ 55 years) who were diagnosed in 1 of 5 Boston hospitals were enrolled. Patient interviews and medical record abstracts provided the information necessary to construct the Charlson index, Satariano index, and a new interview-based index of cardiopulmonary comorbidity. Those indices were used alone and in combination to predict the patient outcomes.

RESULTS. The indices of comorbidity corresponded well with one another. No index of comorbidity predicted mortality or receipt of definitive primary therapy. The new interview-based index of cardiopulmonary comorbidity was a better predictor of upper body function and overall physical function than was the interview-based or medical record-based Charlson or Satariano indices of comorbidity.

CONCLUSION. Older breast cancer patients are able to provide information about their diseases and related symptoms that correlates well with medical record-based measures of comorbidity and displays similar patterns of predictive power. A new self-reported measure of cardiopulmonary comorbidity performs better than the medical record-based measures for predicting patient related functional outcomes.

Key words: epidemiologic factors-comorbidity; breast neoplasms. (Med Care 1999;37: 339–349)

Interest in explaining and reducing sources of variation in medical care has burgeoned, fueled by increasing concerns about the costs, quality, and outcomes of care. Critical to the discourse is the accurate measurement of comorbid or co-existent diseases, as they may influence both the processes and outcomes of care. For example, studies conducted throughout the world over the past decade have documented that breast cancer care for women ≥ 65 years differs substantially from that of younger postmenopausal women, with differences being most pronounced between those ≥ 75 years and their younger counterparts.[1–11] Because the questions of interest have been the relationships between age and appropriate breast cancer therapy, as well as between age and mortality, statistical adjustment for comorbidity has been critical. The most popular methods of comorbidity measurement derive from medical-record or claims based counts of medical conditions, with or without weighting for severity. With appropriate treatment as the outcome, comorbidity has failed

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repeatedly to completely explain age-associated variations in treatment.[3,6,8,10,11] Furthermore, comorbidity has been found to vary in its relationship to survival.[6,12–14]

Interest in quality of life outcomes,[15] as well as the recognition that older women represent the largest group of breast cancer survivors[16] have provided new reasons for the accurate measurement of comorbidity in older women. Such measurement can help disentangle the effects of breast cancer treatment from those related to underlying diseases. Although the medical record and claims based approaches have their strengths, they also have important limitations. Medical-record review is costly and concerns about patient confidentiality are beginning to limit investigators' access to medical records. Furthermore, medical records may incompletely capture patient symptoms; this is certainly the case when relying on claims data. Although the claims-based approach is less expensive than medical record review, the rapid migration of older persons into managed care plans that do not submit claims to Medicare increasingly limits its applicability. Finally, claims information is generally insufficient to answer important questions about patterns of care, particularly in relation to treatments not covered by Medicare (eg, tamoxifen) and health outcomes other than mortality.

Because of those limitations, we and others have begun to evaluate the use of interview-based reports of comorbidity.[11,17–20] Studies comparing interview-based versus medical record-based information are promising. In this paper, we compare interview-based and medical-record based measures of comorbidity and their relation to a range of patient outcomes, including primary tumor therapy and all cause mortality, as well as self-reported upper body and overall physical function.

Methods

Sampling

Details of the study have been described elsewhere.[11] We studied women ≥ 55 years of age with newly diagnosed stage I and stage II invasive breast carcinoma who were cared for at 1 of 5 hospitals in Boston, Massachusetts. Women were ineligible if they had a history of another cancer diagnosis within the previous 5 years or had any prior history of breast cancer. Study participants were sent an introductory letter signed by their surgeon and a consent form at approximately 2 to 3 months following definitive surgical treatment. An interviewer further explained the study, answered questions, and obtained informed consent.

Data Collection

Data were collected from patients' medical records and through a 35 minute computer-assisted telephone interview with consenting eligible patients. Data collected from medical records included the following: tumor size, axillary node status, breast surgery or surgeries performed (mastectomy or breast conserving surgery, with or without axillary dissection), receipt of post-operative radiation therapy, and whether the patient had any of a series of specified co-existing conditions: hypertension, congestive heart failure, angina, previous myocardial infarction, emphysema, chronic bronchitis, asthma, stroke, dementia, Parkinson's disease, diabetes mellitus, and thyroid disease. Co-existing conditions other than those specified were also recorded. All information about co-existing conditions was abstracted from surgeons' initial visit notes, that is, before surgical therapy. The patient telephone interview ascertained demographic variables, the SF-36 Health Survey,[21] diagnoses made by a physician of the same specified co-existing conditions collected from the medical records, and symptoms of cardiopulmonary diseases.

Major Analytic Variables

Dependent Variables. Our first dependent variable was a dichotomous variable representing whether or not women received definitive primary tumor therapy for their breast cancer. We defined definitive therapy as modified radical mastectomy or breast conserving surgery with axillary dissection and radiation therapy.[22,23] Our second dependent variable was the time to death from any cause. For this preliminary analysis, we ascertained deaths among the population from reports of next-of-kin and by matching the identification of patients who had been lost to interview follow up against the state's death records through May 14, 1998. For our quality of life outcomes, we considered both a breast cancer-specific as well as a

general measure of physical function. Our breast cancer-specific measure was a dichotomous variable representing decline in upper body function in relation to breast cancer treatment. Patients were classified as having a decline in upper body function in relation to their breast cancer treatment if: 1) they reported having no difficulty in performing any of three tasks requiring upper body function before treatment and reported that any of those tasks were somewhat difficult, very difficult, or that they did not do the task in the four weeks before interview; 2) they reported that performing any of the three tasks requiring upper body function was somewhat difficult before treatment, and reported that the same tasks were very difficult or that they did not do the tasks, in the 4 weeks before interview; or 3) they reported that performing any of the 3 tasks was very difficult before treatment, and that they did not do the same tasks in the 4 weeks before interview. Patients who did not meet any of these classifications were categorized as having no treatment-related decline in upper body function. Our measure of general function was the continuous physical function index (PFI10) from the SF-36 Health Survey,[21] which was administered to patients at their baseline interview.

Independent Variables. We constructed 5 different measures of comorbidity. Table 1 compares the diseases included in each measure. The first index was a self-reported measure of cardiopulmonary comorbidity derived from the Total Illness Burden Index.[17] The larger Total Illness Burden Index includes measures of 15 different disease categories. We chose to assess the subset of cardiopulmonary items because we thought that from a clinical perspective they were most likely to be related to the outcomes of interest. To derive the cardiopulmonary comorbidity score, individual scores are assigned to ischemic heart disease, chronic obstructive pulmonary disease, and congestive heart failure (Fig. 1).

Second, we constructed the Satariano index of comorbidity[12] from the medical record abstract and from the subject's interview. This index includes as comorbid conditions myocardial infarction, other types of heart disease (valvular disease, arrhythmia, and congestive heart failure), diabetes mellitus, other forms of cancer, and respiratory, liver, and gallbladder conditions. The score was then collapsed into categories of 0, 1, 2, or 3+ conditions as described by the developers of the index.[12] Dummy variables representing each nonzero category were included in the multivariate regression models. Our medical record-based Satariano index differed from the original index only in that we did not record histories of other cancers.[12] Women were ineligible for our study if they had a history of another cancer within 5 years of the breast cancer diagnosis and if they had any history of another breast cancer. Our patient interview-based Satariano index did not include diagnoses of gall bladder disease or liver disease because the interview did not ask about those conditions. By medical record review, 27 patients had gall bladder disease and 4 patients had liver disease.

Third, we constructed the Charlson index of comorbidity[13] from the medical record information and from the subject's interview. That index includes as comorbid conditions myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, ulcer disease, liver disease, diabetes mellitus, malignancies, and AIDS. Weights are given to conditions with greater severity (eg, diabetes mellitus with end organ damage receives a weight of 2 and moderate or severe liver disease receives a weight of 3). In this scoring scheme, weighted scores were then categorized as 0, 1 to 2, 3 to 4, or 5+, as described by the developers of the index.[13] Dummy variables representing each nonzero category were included in the multivariate regression models. Our medical record-based Charlson index differed from the original index in that we could not include the higher order conditions weighted most heavily by Charlson because we did not collect those measures of severity. Given the nature of the higher order conditions and of the study population, we expect that our approximation would differ little from the Charlson comorbidity index for most subjects. Our subject interview-based Charlson index also did not include dementia, peptic ulcer disease, or liver disease because the interview did not ask about those conditions. By medical record review, 1 patient had dementia, 4 patients had peptic ulcer disease, and 4 patients had liver disease.

Confounding Variables. We included the following potential confounding variables in our multivariate models: age; education ($<$ high school vs. $\geq$ high school); living arrangement (living alone vs. living with one or more household members); marital status (married or living with someone vs. any other); body mass index (BMI,

TABLE 1. Diseases Included in the Cardiopulmonary Comorbidity Index, the Satariano Index of Comorbidity, and the Charlson Index of Comorbidity

Cardiopulmonary Comorbidity Index*	Satariano Index	Charlson Index†
Ischemic heart disease	Myocardial infarction	Myocardial infarction
Congestive heart failure	Other types of heart disease, including congestive heart failure	Congestive heart failure
Chronic obstructive pulmonary diseases	Respiratory conditions, including chronic obstructive pulmonary disease	Chronic pulmonary disease
	Diabetes, cancer (other than index diagnosis)‡	Diabetes
	Gall bladder conditions,§ and liver conditions§	Mild liver disease,# peripheral vascular disease, cerebrovascular disease, dementia# connective tissue disease, and peptic ulcer disease#

* See Figure 1 for a more detailed description of the cardiopulmonary comorbidity index, including a description of its modification by symptoms.

† Only the conditions with a weight of 1 are included in the description. More severe comorbid conditions, which were weighted more heavily by Charlson et al, are not included here.

‡ Not included in the Satariano index derived from medical records in this study.

§ Not included in the Satariano index derived from the patient interview in this study.

Not included in the Charlson index derived from the patient interview in this study.

self-reported weight in kilograms divided by height in meters squared); tumor stage (stage I vs. stage II); primary breast cancer therapy (mastectomy versus breast conserving surgery and radiation therapy, not included when appropriate therapy was the dependent variable); axillary node evaluation (performed or not, not included when appropriate therapy was the dependent variable); and days to baseline interview from date of definitive surgery.

Analytic Strategy

To assess the correspondence between the measures of comorbidity, we calculated the correlation between all possible pair wise combinations of the 5 measures of comorbidity. For this analysis only, the Charlson and Satariano indices were included as continuous measures.

For each dependent variable, we constructed a multivariate model that included the confounding variables. For the dichotomous dependent variables, we used logistic regression as the multivariate technique. For the continuous dependent variable (PFI10), we used linear regression as the multivariate technique. For the survival analysis, we used proportional hazards regression as the multivariate technique. After including the confounding variables, we first added the cardiopulmonary comorbidity variable; we, then, added the cardiopulmonary comorbidity variable in combination with the Satariano or Charlson dummy variables. We determined whether the cardiopulmonary comorbidity variable adequately explained the variance of the dependent variable caused by comorbid disease status by calculating the P value associated with the improvement in model fit engendered by adding the Satariano or Charlson variables. In cases in which the addition of the Satariano or Charlson variables significantly improved the model fit, we compared the standardized coefficients of the cardiopulmonary comorbidity score and an ordinal variable representing the Satariano or Charlson index to determine which measure of comorbidity was the most strong predictor of the dependent variable. We conducted the analysis first with the Charlson and Satariano indices derived from the medical record and then repeated the analysis with those indices derived from the subject interviews.

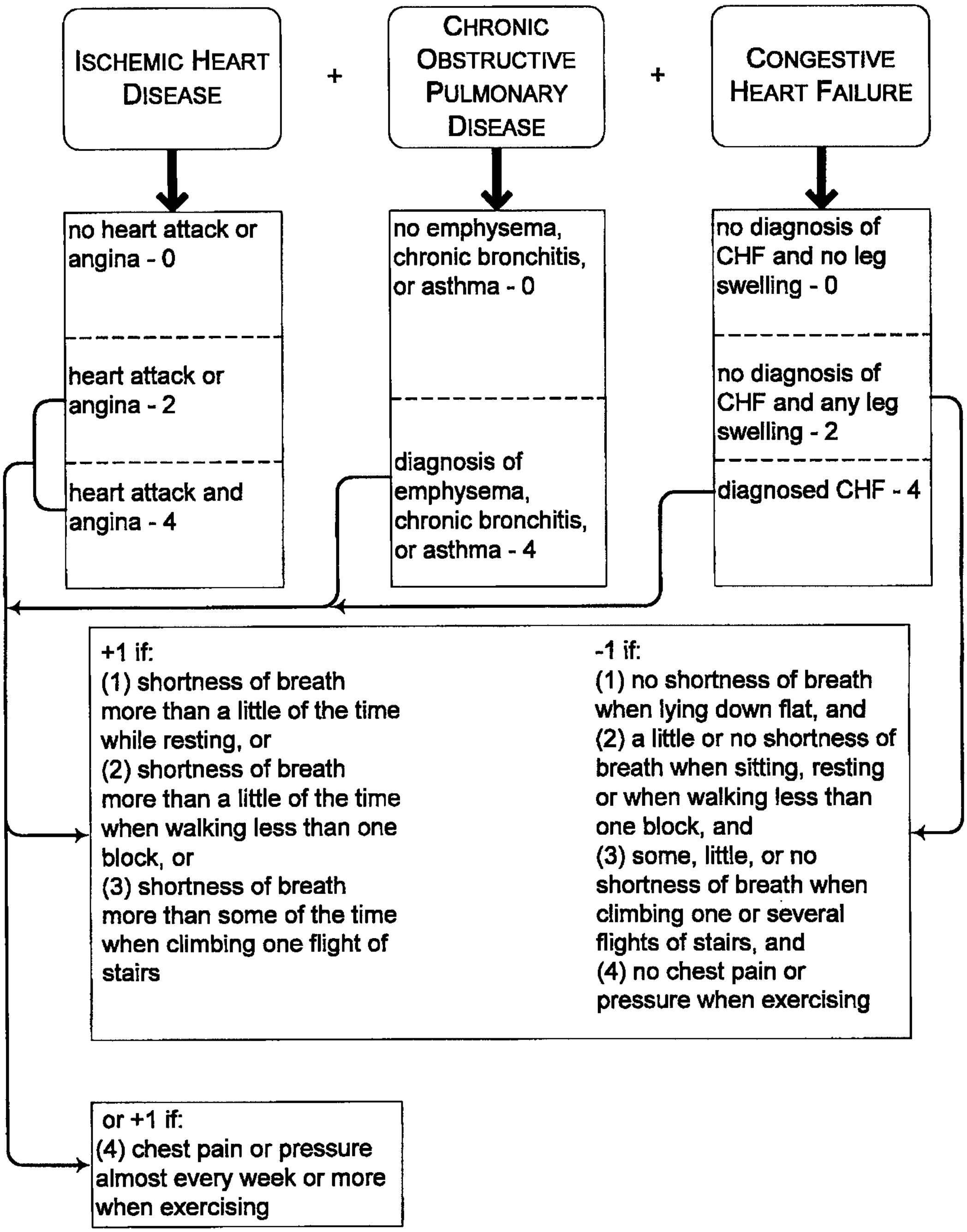

FIG. 1. Derivation of the cardiopulmonary comorbidity score from patient interview responses.

Results

We enrolled 303 patients during the study period (Table 2). Most of the women (83%) had at least a high school education. Two thirds of the women had stage-I breast cancer, the rest had stage-II disease. The majority of the women (64%) received breast conserving surgery and radiation therapy for their primary treatment, and 85% had an axillary node dissection. Three quarters of the

TABLE 2. Distributions of Patient Characteristics

Characteristic	Number	Percent
Age at diagnosis		
55–64	126	41.6
65–74	111	36.6
75+	66	21.8
Education		
<12 years	51	17.0
≥12 years	249	83.0
Living arrangement		
Alone	103	34.3
With 1 or more	197	65.7
Marital status		
Married or living with someone	148	49.2
All other	152	50.8
Body mass index (kg/m^2)		
≤23	91	30.5
>23 to ≤27.5	120	40.3
>27.5	87	29.2
Breast cancer stage		
Stage I	193	63.9
Stage II	109	36.1
Axillary node dissection		
Yes	258	85.4
No	44	14.6
Primary tumor therapy		
Breast conserving surgery and radiation therapy	195	64.3
Mastectomy	71	23.4
Other	37	12.2
Radiation therapy		
Yes	206	68.0
No	97	32.0
Appropriate therapy		
Yes	234	77.2
No	69	22.8
Days between definitive surgery and interview		
1–100	28	9.2
101–130	138	45.5
131–160	74	24.4
>161	63	20.8
Upper body function decline		
Yes	106	35.6
No	192	64.4
Physical function index (scaled 0–100)		
0–25	13	4.4
26–50	37	12.4
51–75	86	28.4
76–100	162	53.5
Vital status		
Died from breast cancer	13	4.3
Died from other than breast cancer	5	1.7
Death certificate not located	6	2.0
Alive	279	92.1

cases met our standards for definitive primary tumor therapy. Most (75%) of the baseline interviews occurred between 100 and 160 days after the patient's definitive surgery.

About one third of the patients suffered some decline in upper body function by the date of their interview. Seventeen percent scored below 50, on a scale from 0 to 100, on the SF-36 Health Survey index of physical function. We located death certificates for 18 of 24 patients lost to follow up as a result of death. Thirteen of 18 deaths were attributed to the patient's breast cancer on the death certificate.

The average of the interview-based comorbidity score increased regularly as the Charlson and Satariano indices increased (Table 3), indicating good correspondence on average between those 3 methods of rating the patient's comorbid disease status. The correspondence held whether the Charlson and Satariano indices were derived from medical records or from subject interviews. The pair-wise correlations between the continuous measures of each comorbidity index further demonstrates the correspondence (Table 4). The correlation coefficient of the cardiopulmonary comorbidity index with the medical record Charlson index was 0.45 ($P \leq 0.001$), with the medical record Satariano index was 0.52 ($P \leq 0.001$), with the patient interview Charlson index was 0.75 ($P \leq 0.001$), and with the patient interview Satariano index was 0.73 ($P \leq 0.001$). Although those measures of comorbidity are highly correlated, the correlations between the continuous measure of cardiopulmonary comorbidity index and the categories of the Charlson or Satariano indices are not

TABLE 3. Relationships between the Charlson and Satariano Indices and Interview-Based Index of CC

	CC Mean ± SD	CC SEM	Range of CC	Number of Subjects
Satariano index group				
Medical record derived				
Zero	0.74 ± 1.44	0.10	0–8	205
One	2.21 ± 2.80	0.32	0–13	77
Two	4.89 ± 3.31	0.78	0–10	18
Three or more	10.00 ± 8.66	5.00	0–15	3
Satariano index group				
Patient interview derived				
Zero	0.49 ± 1.04	0.07	0–6	225
One	3.37 ± 2.64	0.34	0–10	59
Two	6.44 ± 3.68	0.87	1–15	18
Three or more	15		15	1
Charlson index group				
Medical record derived				
Zero	0.91 ± 1.80	0.12	0–13	237
One or two	3.08 ± 3.04	0.39	0–11	62
Three or four	8.50 ± 7.68	3.84	0–15	4
Five or more				0
Charlson index group				
Patient interview derived				
Zero	0.38 ± 0.81	0.06	0–5	214
One or two	3.61 ± 2.70	0.29	0–11	85
Three or four	12 ± 3.61	2.08	8–15	3
Five or more	15		15	1

CC, cardiopulmonary comorbidity; SEM, standard error of mean.

so strong so as to prevent including both the CC index and the categories of either the Charlson or Satariano index simultaneously in a multivariate model.

Table 5 shows the predictive power of the cardiopulmonary comorbidity measure for each of the dependent variables. In addition, it shows the *P* value associated with the improvement in the model fit contributed by the categorized Charlson or Satariano comorbidity index in combination with the cardiopulmonary comorbidity measure. The measures of association between each index of comorbidity and each dependent variable, as well as the standardized coefficients, are available from the authors.

The cardiopulmonary measure of comorbidity did not predict the receipt of definitive therapy. Furthermore, none of the other 4 measures of comorbidity added significant predictive power to the model.

Perhaps because of the short follow-up time and our inability to segregate decedents by cause of death, none of the measures of comorbidity predict mortality. Furthermore, a follow-up will likely yield sufficient numbers of decedents to allow a more thorough examination of those relationships.

The interview-based cardiopulmonary comorbidity measure did predict upper body dysfunction. None of the other 4 measures of comorbidity added significant predictive power to the model after the cardiopulmonary comorbidity score was included.

Finally, the interview-based cardiopulmonary comorbidity measure strongly predicted the physical function subscale of the SF36 when entered in the multivariate models. The negative coefficients shown in Table 5 for the physical function index indicate that increasing cardiopulmonary comorbidity is associated with declining physical function. All comorbidity measures, except for the

TABLE 4. Correlation Coefficient (*P* value) Between Pair-Wise Combinations of the Continuous Indices of Comorbidity

	Cardiopulmonary Comorbidity	Medical Record Charlson	Medical Record Satariano	Patient Interview Charlson	Patient Interview Satariano
Cardiopulmonary	1.0	0.45	0.52	0.75	0.73
Comorbidity	—	(≤0.001)	(≤0.001)	(≤0.001)	(≤0.001)
Medical record		1.0	0.68	0.58	0.58
Charlson		—	(≤0.001)	(≤0.001)	(≤0.001)
Medical record			1.0	0.55	0.60
Satariano			—	(≤0.001)	(≤0.001)
Patient interview				1.0	0.87
Charlson				—	(≤0.001)
Patient interview					1.0
Satariano					—

medical-record derived Satariano index, significantly improved the model fit when added to the multivariate model that included the cardiopulmonary comorbidity score. This observation suggests that the cardiopulmonary comorbidity index did not fully explain the relation between increasing comorbidity and declining function. In each model, though, the standardized coefficient of the cardiopulmonary comorbidity score indicated that it was a more powerful predictor than the Charlson or Satariano indices, regardless of whether they derived from the medical record or from the patient interview (data not shown, but available from the authors upon request). Therefore, if one could choose only a single measure of comorbidity to predict physical function, the cardiopulmonary comorbidity index would be preferred, at least, in this population.

Discussion

In this comparison of various methods and sources of comorbidity measurement, we found that, regardless of the method or source, no measure of comorbidity was statistically significantly associated with the receipt of definitive primary tumor therapy. In other studies the observed relationship between comorbidity and primary tumor therapy has varied. Although Greenfield et al found that comorbidity and age were independently and significantly associated with definitive treatment among women 50 years or older,[3] Bergman found that advanced age (≥ 75 years) was a better predictor of treatment than was comorbidity.[6] Both studies relied on medical record-based measures of comorbidity. Similarly, in studies using claims-based Charlson indices, Newschaffer et al found that comorbidity had no relationship to surgical or radiation therapy,[10] whereas Ballard-Barbash found modest relationships between comorbidity and both surgical and radiation therapies after controlling other potentially confounding factors.[8] In both the Newschaffer and Ballard-Barbash studies, patients in the oldest age groups were less likely to receive these therapies, independent of all other measured variables.[8,10]

Although it is not central to this investigation, our findings and those of others lead us to conclude that considerations of comorbidity do not completely drive therapeutic decisions regarding primary tumor therapy and do not explain the relationship between age and treatment patterns, regardless of the method of comorbidity measurement. Nonetheless, adequate measurement of comorbidity should be required of all studies of age associated variations in breast cancer care. Here adequacy of measurement should be defined in terms of the risks and benefits of therapy. Thus, a measure of cardiopulmonary comorbidity may well be adequate for studies of surgical and/or radiation therapy. However, studies of adjuvant chemotherapy would need to include laboratory measures of renal and hepatic function.

Although attention to the measurement of comorbidity is important in studies of age-associated

TABLE 5. Relationships Between the Dependent Variables and the Index of Cardiopulmonary Comorbidity, Controlling for the Charlson or Satariano Index of Comorbidity

Dependent Variable	Model	Relative Risk or Change in PFI10 Associated With a Unit Increase in CC (95% CI)	*P* Value Associated With Addition of Charlson or Satariano Index
Receipt of less than appropriate primary tumor therapy	CC alone	1.03 (0.91, 1.16)	Not applicable
	CC + MR* Charlson	0.97 (0.85, 1.11)	0.10
	CC + MR Satariano	1.02 (0.88, 1.17)	0.94
	CC + PI† Charlson	0.98 (0.81, 1.19)	0.24
	CC + PI Satariano	0.93 (0.78, 1.12)	0.39
All cause mortality	CC alone	0.84 (0.65, 1.09)	Not applicable
	CC + MR Charlson	0.84 (0.64, 1.11)	0.95
	CC + MR Satariano	0.85 (0.64, 1.12)	0.98
	CC + PI Charlson	0.84 (0.60, 1.17)	0.99
	CC + PI Satariano	0.89 (0.64, 1.24)	0.78
Upper body dysfunction	CC alone	1.16 (1.04, 1.30)	Not applicable
	CC + MR Charlson	1.13 (0.99, 1.27)	0.18
	CC + MR Satariano	1.14 (1.00, 1.31)	0.34
	CC + PI Charlson	1.12 (0.95, 1.33)	0.39
	CC + PI Satariano	1.14 (0.97, 1.34)	0.20
Physical function index (PFI10)	CC alone	−2.56 (−3.43, −1.68)	Not applicable
	CC + MR Charlson	−2.26 (−3.23, −1.30)	0.001
	CC + MR Satariano	−2.65 (−3.68, −1.62)	0.142
	CC + PI Charlson	−2.41 (−3.78, −1.04)	0.063
	CC + PI Satariano	−2.75 (−4.03, −1.48)	0.002

CC, cardiopulmonary comorbidity index.
* MR, derived from the patient's medical record.
† PI, derived from the patient's interview.

variations in breast cancer care, equal attention should be given to alternative explanations. For example, a patient's functional status is likely to be important, because comorbidity and functional status are known to contribute unique information to our understanding of the health status of older persons.[24–26] However, studies that have controlled for functional status, either based on medical record information[3] or patient's self report[11] have found that age persists as an independent predictor of treatment. The lack of association may reflect the need for more detailed measures of functional status, and further studies are needed that measure functional status more comprehensively. Additional studies are also needed to more adequately explore the roles of physician attitudes and fully informed patient preferences as predictors of treatment.

With respect to mortality, none of our comorbidity measures was associated; that may be because the number of deaths in our sample is, as yet, small. Newschaffer et al recently compared Medicare claims versions of the Charlson and Satariano indices with their medical record-based versions in a sample of women (≥ 67 years) who were newly diagnosed with breast cancer. Although the claims-based and medical record-based methods had poor agreement, indices derived from both sources were modestly (odds ratios of 1.28–1.53) associated with 3 to 5 year all cause mortality, controlling for age, stage, and treatment. The Charlson claims-based score added modest prediction over the Charlson medical record-based score.[6]

Finally, we found that patient self-report of cardiopulmonary comorbidity was a better predic-

tor of breast cancer specific as well as general physical function than were either the medical record- or patient interview-based Satariano and Charlson indices. The fact that neither the medical-record nor patient-interview based Satariano and Charlson measures performed as well suggests that the observed relationships are not caused by measurement source (ie, medical record vs. patient). In cases in which symptoms reflect disease severity, patients may be a better source of information than their physicians. Indeed, in comparison with patients' report of cardiopulmonary comorbidity, both the Satariano and Charlson, regardless of source, underestimated comorbidity 32% to 34% of the time. This may partially be because neither method takes into account the contribution of symptoms. For example, in the Charlson index, severe pulmonary and cardiac disease receive the same weighting as do mild forms of these diseases.[13]

Studies comparing medical records and patient self report suggest that patients are most accurate when asked about well defined conditions, such as heart disease or diabetes mellitus and least accurate for less well defined conditions such as arthritis.[17,18] Older age and less education have been variably associated with lower agreement between medical records and self report.[18–20] Thus, studies in which well defined diseases are critical and/or in which patient symptoms are relevant, patient self reports of diseases and symptoms may be sufficient, if not superior, for the measurement of comorbidity. That approach may be particularly useful in circumstances in which missing data in medical records are common.

Although our findings are promising, they must be viewed with several limitations in mind. First, the women in our study were mostly White and well educated. Nonetheless, they ranged in age up to 97, so included women at greatest risk for a large burden of comorbid conditions. Second, we did not construct our data collection instruments to fully represent the Satariano and Charlson indices. Thus, some of the underestimation of those measures may be related to incomplete data collection. The medical record-based Charlson index consistently underestimated diagnoses as identified by a complete ascertainment through patient interview in a similar study.[20] The interview-based Charlson and Satariano indices may, therefore, balance the incomplete assessment of diseases with a more complete ascertainment of the diseases that were assessed. Third, our sample size was relatively small and resulted in imprecise estimates of effect. Fourth, the small number of deaths preclude definitive statements about the relationship between our various comorbidity measures, and all cause mortality.

Nonetheless, we believe that our data support several conclusions. First, older breast cancer patients are able to provide information about their diseases and relate symptoms that correlate well with medical record-based measures and displays similar patterns of predictive power. Second, our self-reported measure of cardiopulmonary comorbidity performs better than our medical record-based measures in the prediction of patient-related functional outcomes. Continued refinement of this approach offers promise for the efficient and valid measurement of comorbidity.

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The Care of Older Women with Early Stage Breast Cancer: What is the Role of Surgeon Gender?

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The Care of Older Women with Early Stage Breast Cancer:

What is the Role of Surgeon Gender?

Abstract

Background. - Over the past decade and a half a substantial literature has documented age-dependent variations in breast cancer care. Accumulating evidence suggests that these variations do impact the health outcomes of older women with breast cancer. Surgeon gender may be an important source of age-dependent variations in care.

Objective. - To examine the relationship between surgeon gender and primary tumor therapy and systemic adjuvant therapy among 303 older women with early stage breast cancer cared for by 20 surgeons in Boston, Massachusetts.

Research Design. - Cross-sectional observational study.

Subjects. - Women at least 55 years of age with newly diagnosed stage I or II breast cancer.

Main Outcome Measure. - Definitive primary tumor therapy and systemic adjuvant therapy.

Results. - After adjustment for patient and tumor characteristics, patients of female surgeons were more likely to receive definitive treatment, with the strongest effect being observed for the receipt of both definitive primary tumor therapy and systemic adjuvant therapy (OR 4.5; 95% CI 2.7, 7.7).

Conclusions. - Women with early stage breast cancer cared for by female surgeons are more likely to receive standard therapies. Surgeons provide the initial care for all women with breast cancer – both diagnostic as well as therapeutic care. Their role in breast cancer care is pivotal and has a substantial impact on the nature of breast cancer care received.

Abstract Word Count: 223

Introduction

Over the past decade and a half, a substantial literature has documented age-dependent variations in breast cancer care (1-13). Although some aspects of care have changed over this period of time (*e.g.*, breast conserving surgery has increased), age-dependent variations have persisted into the 1990's (13). The next level questions are 1) Do these variations make a difference with respect to important health outcomes? If so, 2) What are the reasons for these variations?

Accumulating, albeit incomplete, observational evidence suggests that age-dependent variations do impact the health outcomes of older women with breast cancer. Specifically, studies from the United States and Italy have identified both higher recurrence rates and higher mortality rates among women who receive less than definitive primary tumor therapy (14-16). Furthermore, breast cancer-specific mortality rates are declining among women less than 70 years old, but are either stable (70-79 year olds) or increasing (80 + year olds) among those 70 years of age or older (17). Increasing rates of screening mammography and better treatment regimens may partially explain declining mortality rates among women less than 70 years old. Although screening mammography rates decline progressively with age, there is no evidence to suggest that the diagnosis of late stage disease among the oldest women has been increasing over time or that there have been systematic changes in the attribution of breast cancer as the cause of death (17). This leaves the receipt of less than definitive treatment as the better explanation for why mortality rates among older women are increasing, particularly among those aged 80 years or older (17). This contention is supported by the available age-specific clinical trial data that fail to demonstrate that treatment efficacy is modified by age (18-20).

The quality of the medical encounter may be an important source of age-dependent variations in breast cancer care. Studies of physician-patient interactions have demonstrated that the quality of physician-patient interactions decreases with patient age. Physicians spend less time with their older patients than they do with their younger patients (21, 22). Physicians also provide better information and support to their younger patients than to their older patients (23). These physician behaviors are compounded by the behaviors of older patients themselves. In general, older patients are less assertive and defer more to their physicians than do younger patients (24). Indeed, a recent study of over 1000 women with breast cancer found that 48% of women ≥ 70 years of age preferred to have a passive role in decision-making, compared with 36% of those 50-69 years, and 21% of those < 50 years of age (25).

Gender issues may accentuate the effects of these age-related behaviors. Because of gender disparities in life expectancy, most older patients are women. Until recently, most physicians were men. The latter circumstance is changing rapidly and a growing literature has documented differences between male and female physicians, both in their styles of interactions as well as in the care that they deliver. For example, compared with male physicians, female physicians engage in more question-asking and information-giving (26). The longest visits are between female physicians and their female patients; the shortest visits are between male physicians and their female patients (26). Although several studies have documented that women are more likely to undergo cervical and breast cancer screening if they see female rather than male physicians (27-29), no study has documented that breast cancer care is similarly influenced.

As part of a study of age-related variations in breast cancer care (13), we examined the relationship between surgeon gender and primary tumor therapy and systemic adjuvant therapy

among older women with early stage breast cancer cared for by seven female surgeons and thirteen male surgeons in Boston, Massachusetts. We sought to determine whether surgeon gender was associated with the receipt of primary tumor and systemic adjuvant therapy, once relevant patient and physician characteristics had been considered.

Methods

Data Collection

The study's methods have been described elsewhere (13). Participating women were at least 55 years old and newly diagnosed with stage I or II breast cancer. They received their initial breast cancer care from surgeons in office-practice settings affiliated with one of five academic medical centers in Boston, Massachusetts. These settings included general surgery private practices and interdisciplinary breast health care centers. Data were collected from women's medical records, a 35 minute computer-assisted telephone interview with consenting women, and the Massachusetts Physician Profiles database of the Board of Registration in Medicine of the Commonwealth of Massachusetts (30). Data collected from medical records included stage, estrogen receptor status, surgeries performed, and additional therapies received (radiation therapy, chemo- and/or hormonal therapy). Medical records were monitored for six months to determine whether radiation therapy and chemotherapy were initiated and completed or discontinued, and whether hormonal therapy was initiated. The patient telephone interview included questions about sociodemographic characteristics (age, race, marital status, education, and income); general health-related quality of life; the presence of physician-diagnosed cardiopulmonary diseases and the frequency of associated symptoms; and ratings of aspects of physician-patient interactions. We obtained training information about surgeons from the

Massachusetts Physician Profiles database (30), including year graduated from medical school, board certification in general surgery, and fellowship training in surgical oncology.

Major Analytic Variables: Our dependent variable had two components: 1) definitive primary tumor therapy, categorized as "yes" if the patient received either modified radical mastectomy or breast conserving surgery with axillary dissection followed by radiation therapy, otherwise "no"; and 2) systemic adjuvant therapy, categorized as "yes" if the patient received either chemotherapy or hormonal therapy alone, or in combination, otherwise "no." These two components were then combined to form a four level variable: no/no, no/yes, yes/no, and yes/yes, reflecting the receipt of various combinations of definitive primary tumor therapy and systemic adjuvant therapy.

Our independent variable of interest was surgeon gender (female/male). We considered as covariates (1) patient characteristics that have previously been shown to be associated with treatments received by older women with newly diagnosed early stage breast cancer: age (1-13), race (31), marital status (13), socioeconomic status [education and income] (7, 31), comorbidity (2, 6, 8), functional status (2), and physician-patient communication (13); (2) clinically important prognostic factors that should influence treatment decisions: tumor characteristics (stage [I/II], estrogen receptor status [positive/negative], and risk of recurrence; and (3) surgeon characteristics that might explain the relationship between surgeon gender and treatment received: years since graduation from medical school [≤ 15 years/>15 years] and whether they practiced at a breast health center [yes/no]. Patients' demographic characteristics included age (55-64, 65-74, 75-84, and 85+ years), marital status (married, widowed, and single, separated, or divorced), education (< high school, high school, some college, and college graduate), and annual household income (≤ $14,999, $15 - 29,999, $30 - 49,999, and $50,000 +). We measured

comorbidity using patients' reports of diagnoses of chronic obstructive pulmonary disease, congestive heart failure, and ischemic heart disease, and related disease manifestations and symptoms that were part of the Total Illness Burden Index (32). We assessed physical function using the 10-item physical function subscale of the Medical Outcomes Study SF-36, which is scaled from 0-100 with a higher score indicating better function (33). In the analysis we also considered comorbidity and physical function as four-level ordinal variables, dividing the sample into four approximately equal groups. We categorized node-negative women as being at low, intermediate, and high risk of recurrence based on tumor size and estrogen receptor status (34), and node positive women as being at high risk of recurrence. Our measure of patients' perceptions of their own abilities to communicate with their physicians was a three item scale, developed for this study (13, 35), based on patients' ratings of their abilities to get information from, and to give information to their physicians [Cronbach's $\alpha = 0.96$].

Statistical Analysis

We obtained descriptive statistics on all medical record and patient interview variables and then examined the association between the independent variable and covariates, and between these variables and the outcome variable, using analysis of variance and the chi-square test. Variables that were statistically significantly associated with the dependent variable ($p<0.05$) at the bivariate level were candidates for entry into a polytomous logistic regression model, a generalization of the binary logistic regression model to more than two outcome categories (36). Because of cells with zero frequency, we recategorized age as 55-64, 64-74, and 75+ and education as < high school, high school, and > high school for this analysis. Income was not retained in the final model because neither its presence nor absence changed substantially the

parameter estimate associated with surgeon gender, most likely because of its strong association with age, marital status, and education (all p = 0.001).

The polytomous logistic regression model assumes that the outcome variable categories are mutually exclusive. The odds ratio for the independent variable (surgeon gender) at a given outcome level (*e.g.*, yes/yes) represents the odds of receiving yes/yes over receiving no/no among patients cared for by female surgeons compared to those cared for by male surgeons (37). In choosing this analytic strategy we were concerned about violating the statistical assumption of independence. To address this concern we examined the correlation among patients within surgeon and the observed correlation coefficients were very small (e.g., 0.00, -0.03, 0.04) suggesting that the assumption of independence in the polytomous regression model is valid. We were also concerned that the results observed might reflect one or two surgeon outliers. When we examined the distribution of treatments by surgeon, not only were there no outliers, but the distributions of treatments were similar within female and male surgeon groups

Finally, we also performed a series of stratified analyses to assess whether the treatment patterns represented potential over or undertreatment. In these analyses we examined patterns of care in relation to risk of recurrence by surgeon gender.

Results

Study Sample

Three hundred three women participated in the study. A little more than half (58%) of our subjects were $\geq$ 65 years of age (range 55-97 years) and most were white (93%). About half were married (51%) and the majority had a high school education or more (83%). Their average comorbidity score was 7.06 (range 3-20). The majority of patients had stage I disease (64%). The majority of women in our study also underwent breast conserving surgery and axillary

dissection followed by radiation therapy (56%); less than a quarter received a modified radical mastectomy (22%); the remaining 22% received other therapies. About two-thirds (67%) of the women received some form of systemic adjuvant therapy. Of these, most (76%) received hormonal therapy alone. A much smaller percentage received either chemotherapy alone (13%) or both chemotherapy and hormonal therapy (11%).

The Massachusetts Physician Profiles database provided information about 19 of the 20 surgeons. These surgeons, including 7 women and 12 men, cared for 301 of the 303 patients. A little over half (53%) had graduated from medical school within the past 15 years. All but 1 were board certified in general surgery. Two female surgeons and 2 male surgeons had completed surgical oncology fellowship training.

Patient Characteristics in Relation to Surgeon Gender

Patient characteristics in relation to surgeon gender are displayed in Table 1. As can be seen, the patients cared for by female surgeons were very similar to those cared for by male surgeons with respect to demographic characteristics, health status, tumor characteristics, and abilities to communicate with their physicians. However, male surgeons did care for a higher proportion of women of minority status and with the lowest income.

Patient and Surgeon Characteristics in Relation to Therapies Received

Patient and surgeon characteristics in relation to therapies received are displayed in Table 2. Women who were less than 65 years of age were more likely to receive both definitive primary therapy and systemic adjuvant therapy (yes/yes). Women 85 years of age or older were more likely to receive neither definitive primary therapy nor systemic adjuvant therapy (no/no). No differences were observed as a function of race, although the number of non-white women (n=20) was quite small. Married women, those who were college educated, and those with an

annual household income of $30,000 or more were more likely to receive both definitive primary therapy and systemic adjuvant therapy than those who were not married, had less education, or had lower annual household incomes, respectively. There were no significant differences in treatments received with respect to cardiopulmonary comorbidity or physical function. As expected, women with stage II disease and those who were at higher risk of recurrence were much more likely to receive both definitive primary therapy and systemic adjuvant therapy. However, there were no differences in relation to estrogen receptor status.

There were no significant differences in treatments received related to women's perceptions of their abilities to communicate with their physicians. In addition, no differences were observed with respect to years since the surgeons had graduated from medical school or whether they worked in a breast health care center. However, women cared for by female physicians were more likely to receive both definitive primary therapy and systemic adjuvant therapy, whereas women cared for by male physicians were more likely to receive neither.

Results of our polytomous regression model are displayed in Table 3. In each comparison with the referent outcome group (neither definitive primary tumor therapy nor systemic adjuvant therapy) and controlling for age, stage, education, and marital status, the odds of receiving each of the more definitive treatment combinations were statistically significantly greater among women cared for by female surgeons compared to women cared for by male surgeons, with the strongest effect being observed for the receipt of both definitive primary therapy and systemic adjuvant therapy. Patients cared for by female surgeons were about four and one-half times more likely to receive both therapies compared to those cared for by male surgeons.

With respect to the question as to whether these patterns may represent over or under

treatment, among patients of female surgeons, 60% of those who received neither definitive primary tumor therapy nor adjuvant therapy were at low risk of recurrence. Among patients of male surgeons, 18% of those who received neither definitive primary tumor therapy nor adjuvant therapy were at low risk of recurrence. In contrast, no patients of female surgeons who received neither therapy were classified as being at high risk of recurrence whereas 36% of patients of male surgeons who received neither therapy were at high risk.

Conclusions

In this study of breast cancer care received by older women, we found that surgeon gender was independently associated with the receipt of definitive primary tumor therapy and systemic adjuvant therapy. Our data do not support the contention that the observed relationship is because different kinds of women seek care from female surgeons than seek care from male surgeons (Table 1). In addition, treatment patterns do not differ according to comorbidity and functional status, nor in relation to women's perceptions of their abilities to communicate with their physicians, the recency of their surgeon's training, or the setting in which care is delivered (Table 2). Furthermore, in our polytomous logistic regression analysis (Table 3), the effect of surgeon gender persisted after statistical control for patient age, education, marital status, and tumor stage. Although it is possible that unmeasured factors may be unbalanced across groups of women cared for by female as opposed to male surgeons, this seems unlikely.

Nonetheless, our findings must be interpreted with the study's limitations in mind. First, our older women with breast cancer were mostly middle-class white women from one city in the Northeast United States and the oldest women (85+) were underrepresented due to a higher refusal rate (13). Second, these women were cared for by a relatively small number of surgeons who practiced in settings with academic affiliation. Although we cannot be certain, it is possible

that the variations we observed might have been greater had we studied a more diverse group of women and surgeons. Third, we did not have detailed information about actual clinical encounters between surgeons and patients. This precluded our developing an in-depth understanding of the factors that explain the observed relationship between surgeon gender and therapies received.

In the absence of such information, we suggest the following as a possible explanation for our findings. The lack of an association between comorbidity and therapies received, which has been observed by others (2, 6, 8, 10, 13), in conjunction with the similar lack of association between recency of surgeon training, site of care, and therapies received contradict conventional wisdom. When coupled with the observation that therapies received do vary in relation to surgeon gender, however, they suggest that female and male surgeons may interpret differently the available literature regarding treatment efficacy and effectiveness. We believe that female surgeons may weigh the evidence more carefully and discuss it more comprehensively with their patients. Rather than deciding "what is best" for patients and making assumptions about the importance of factors such as risk of recurrence, out of pocket expenses, and difficulty getting to and from treatments (13), female surgeons may explore more explicitly the weight that women give to these considerations.

In spite of observational study evidence linking variations in primary tumor therapy and patient outcomes, there is considerable controversy surrounding what constitutes appropriate therapy for older women with breast cancer. Radiation therapy following breast conserving surgery as one example. Clinical trials have consistently demonstrated that radiation therapy following breast conserving surgery reduces local recurrence rates by about 20%, regardless of stage (19, 38). Advocates of omitting radiation therapy in older women undergoing breast

conserving surgery argue that clinical trials have not demonstrated that radiation therapy prolongs survival (39). In addition, a few studies suggest that older women may be at decreased risk of local recurrence when compared to their younger counterparts (19). Countering these arguments are the facts that, survival benefits aside, local recurrences may be difficult to manage (especially recurrences to skin); may require additional surgery or radiation therapy for local control; and may be psychologically devastating. Moreover, the apparent lower risk of recurrence may be an artifact of patient selection and of the extent of surgical excision employed (19).

Similar arguments have been made for and against the use of axillary dissection in older women. Axillary dissection has been advocated as a therapeutic intervention because it eliminates residual disease and provides critical stage information. A recent report suggests that women ≥ 65 years of age who do not receive an axillary dissection have impaired survival compared to those who receive definitive therapy (12). With respect to staging, the argument for not subjecting older women to axillary dissection is that a dissection is unnecessary if all older women are prescribed and take tamoxifen. Moreover, axillary dissection is associated with considerable morbidity (40). Countering these arguments is the reality, observed clearly in the study reported herein, that not all older women, including high risk women, receive adjuvant tamoxifen therapy. Furthermore, clinical evaluation of the axillary nodes has a false negative rate that ranges from 15%-35% (41). A potential alternative to axillary dissection is lymphatic mapping and sentinel node biopsy, but the technique may be less useful in older women because the success rate of this technique is lower in them (42).

Although there is controversy regarding the effectiveness of radiation therapy and axillary dissection in older women, the evidence regarding adjuvant tamoxifen therapy is clearer.

The 1998 St. Gallen 6th International Consensus Panel of the Treatment of Primary Breast Cancer recommended that, with the exception of low risk node negative patients (less than a 10% risk of relapse at 10 years), all elderly patients should receive tamoxifen therapy except those who are estrogen receptor negative (43). These recommendations are supported by the meta-analysis update of randomized trials that concluded that five years of tamoxifen therapy substantially reduces the risk of recurrence, mortality, and contralateral disease among women whose tumors are estrogen receptor positive. This benefit is independent of age, node status, and receipt of chemotherapy (18). Although these latter findings were not available when the women studied herein were diagnosed, the 1990 NIH Consensus Conference stated that although "the majority of patients with node-negative breast cancer are cured by breast conservation treatment or total mastectomy and axillary dissection," combination chemotherapy or two years of tamoxifen is recommended (44).

Our data, though limited, support the assertion that some high risk patients may be being undertreated, more often by male surgeons. Whether these treatment patterns will be reflected ultimately in variations in breast cancer-specific outcomes is not known. Outcome studies in this country have not included systemic adjuvant therapy, in part because both the Surveillance, Epidemiology, and End Results program and local tumor registries do not collect such information and because Medicare does not pay for tamoxifen. Addressing important questions about the effectiveness of primary tumor therapy and systemic adjuvant therapy will require longitudinal studies of large numbers of older women that collect detailed treatment information over follow-up periods of at least five years. Such studies are planned or in progress, but data will not be available for some time.

Meanwhile, our findings have implications for the care for older women with breast cancer. Surgeons provide the initial care for all women with breast cancer – both diagnostic as well as therapeutic care. Their discussions with women condition the broadening or narrowing of possible treatment options. Surgeons also facilitate referral to other breast cancer specialists – radiation and medical oncologists. Furthermore, they may be the ones who prescribe tamoxifen and monitor women for side effects and adherence, as well as for symptoms of recurrence. Thus, their role in breast cancer care is pivotal and has a substantial impact on the nature of breast cancer care received.

Our findings are consistent with those of others who have explored gender differences in primary care settings (26, 45). These studies have documented that female physicians are more nurturing and expressive and have a stronger interpersonal orientation than do their male counterparts. In interactions with their female patients they contribute more equally to the interaction, allowing patients to tell their stories (45). This aspect may be particularly important for the current generation of older women patients who are less likely than younger women to be assertive and to ask questions. Regardless of whether or not this is a cohort effect, all women with newly diagnosed breast cancer will be better served by enhancing the quality of physician-patient communication. Thus, rather than recommending that more female surgeons should be trained or that older women with breast cancer should be referred to female surgeons for their care, we believe that greater emphasis needs to be placed on teaching physicians effective communication skills. Although the development of interpersonal skills may come more easily to female physicians in general, all physicians will benefit from interviewing skills training during medical school, during postgraduate training, and beyond (25). The methods for teaching these skills are well-developed and have been shown to be effective (47).

However, unless physicians have more time to talk with and to listen to their patients, such interventions are destined to fail. We need to think creatively about ways to help physicians provide information efficiently and effectively, be it by taking advantage of new technologies or by organizing some aspects of information-sharing with groups of patients (48). This is particularly important because of the increasing time pressures being placed on physicians who care for older patients, who often need more time to comfortably participate in their own health care decisions. Although future generations of older patients may be more assertive and facile with obtaining information from sources other than physicians, when faced with a potentially life threatening disease such as breast cancer they will still want their physicians to spend time and to discuss available options with them.

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TABLE 1. Patient Characteristics and Surgeon Gender

Patient Characteristics	Surgeon Gender Female (n=174)	Male (n=129)	P-Value
Patient Demographics			
Age (years)			
55-64	75 (60%)	51 (40%)	0.74
65-74	65 (59)	46 (41)	
75-84	27 (52)	25 (48)	
85+	7 (50)	7 (50)	
Race			
White	168 (60)	113 (40)	0.001
Non-White	4 (20)	16 (80)	
Marital Status			
Married	84 (57)	64 (43)	0.94
Widowed	56 (57)	43 (43)	
Single/Divorced	32 (59)	22 (41)	
Education			
< High school	26 (51)	25 (49)	0.65
High school	61 (57)	46 (43)	
Some college	45 (63)	27 (47)	
College graduate	40 (57)	30 (43)	
Income[a]			
≤ $14,999	26 (49)	27 (51)	0.018
15,000 - 29,999	44 (73)	16 (27)	
30,000 - 49,999	40 (63)	24 (37)	
50,000+	30 (57)	23 (43)	

TABLE 1. Patient Characteristics and Surgeon Gender

Patient Characteristics	Surgeon Gender: Female (n=174)	Male (n=129)	P-Value
Health Status			
Comorbidity score			
I (lowest quartile)	51 (58)	37 (42)	0.53
II	45 (64)	25 (36)	
III	41 (55)	34 (45)	
IV (highest quartile)	37 (53)	33 (47)	
Physical function score			
I (lowest quartile)	39 (50)	39 (50)	0.18
II	31 (53)	27 (47)	
III	39 (59)	27 (41)	
IV (highest quartile)	63 (66)	33 (33)	
Tumor Characteristics			
Stage			
I	114 (59)	79 (41)	0.41
II	59 (54)	50 (46)	
Risk of recurrence			
Low	42 (67)	21 (33)	0.24
Intermediate	63 (58)	45 (42)	
High	51 (53)	45 (47)	
Communication Skills	70.43	70.98	0.86

[a] Values missing for 73 subjects

TABLE 2. Patient and Surgeon Characteristics and Therapies Received: Definitive Primary/Systemic Adjuvant[a]

Characteristics	No/No (n=22)	No/Yes (n=47)	Yes/No (n=77)	Yes/Yes (n=157)	P-value
Patient Demographics					
Age (years)					
55-64	5 (4%)	8 (6%)	35 (28%)	78 (62%)	0.001
65-74	8 (7)	10 (9)	28 (25)	65 (59)	
75-84	4 (8)	23 (44)	11 (21)	14 (27)	
85+	5 (36)	6 (43)	3 (21)	0 (00)	
Race					
White	20 (7)	41 (14)	72 (26)	148 (53)	0.55
Non-White	2 (10)	5 (25)	5 (25)	8 (40)	
Marital Status					
Married	6 (4)	12 (8)	44 (30)	86 (58)	0.001
Widowed	13 (13)	22 (22)	18 (18)	46 (47)	
Single/Divorced	3 (6)	12 (22)	15 (28)	24 (44)	
Education					
< High school	10 (20)	11 (21)	10 (20)	20 (39)	0.002
High school	8 (5)	14 (13)	26 (24)	59 (55)	
Some college	0 (0)	12 (17)	26 (36)	34 (47)	
College graduate	4 (6)	8 (12)	15 (21)	43 (61)	
Income[b]					
≤ $14,999	7 (13)	17 (32)	12 (23)	17 (32)	0.001
15,000-29,999	5 (8)	4 (7)	19 (32)	32 (53)	
30,000-49,999	0 (0)	5 (8)	15 (23)	44 (69)	
50,000+	2 (4)	5 (9)	12 (23)	34 (64)	

TABLE 2. Patient and Surgeon Characteristics and Therapies Received: Definitive Primary/Systemic Adjuvant[a]

Characteristics	No/No (n=22)	No/Yes (n=47)	Yes/No (n=77)	Yes/Yes (n=157)	P-value
Patient Health Status					
Comorbidity score					
I (lowest quartile)	4 (5)	15 (17)	22 (25)	47 (53)	0.8
II	4 (6)	10 (14)	19 (27)	37 (53)	
III	7 (8)	9 (12)	16 (21)	43 (57)	
IV (highest quartile)	7 (10)	13 (19)	20 (28)	30 (43)	
Physical function score					
I (lowest quartile)	7 (9)	15 (19)	17 (22)	39 (50)	0.2
II	7 (12)	10 (17)	13 (22)	28 (42)	
III	3 (5)	11 (17)	19 (29)	33 (50)	
IV (highest quartile)	4 (4)	7 (7)	28 (29)	57 (59)	
Tumor Characteristics					
Stage					
I	20 (10)	40 (21)	64 (33)	69 (36)	0.001
II	2 (2)	7 (6)	13 (12)	87 (80)	
Estrogen receptor status					
Positive	12 (6)	34 (16)	48 (23)	116 (55)	0.44
Negative	5 (8)	6 (9)	19 (28)	37 (55)	

TABLE 2. Patient and Surgeon Characteristics and Therapies Received: Definitive Primary/Systemic Adjuvant[a]

Characteristics	No/No (n=22)	No/Yes (n=47)	Yes/No (n=77)	Yes/Yes (n=157)	P-value
Tumor Characteristics					
Risk of recurrence					
Low	5 (8)	13 (21)	26 (41)	19 (30)	0.001
Intermediate	7 (6)	18 (17)	24 (22)	59 (55)	
High	4 (4)	7 (7)	14 (15)	71 (74)	
Communication Skills	69.44	66.88	70.67	72.24	0.57
Surgeon Characteristics					
Years since medical school graduation					
≤ 15 years	15 (7)	34 (16)	52 (25)	106 (51)	0.95
> 15 years	7 (7)	13 (14)	25 (26)	49 (52)	
Gender					
Female	7 (4)	27 (16)	42 (24)	98 (56)	0.05
Male	15 (12)	20 (15)	35 (27)	59 (46)	
Practice site					
Breast Health Center	17 (8)	35 (17)	49 (23)	111 (52)	0.47
Other	5 (5)	12 (13)	28 (31)	46 (51)	

[a] No/No = No definitive primary tumor therapy

No/No = No systemic adjuvant therapy

No/Yes = No definitive primary tumor therapy

Systemic adjuvant therapy

Yes/No = Definitive primary tumor therapy

No systemic adjuvant therapy

Yes/Yes = Definitive primary tumor therapy

Systemic adjuvant therapy

[b] Values missing for 73 subjects

TABLE 3. Polytomous Logistic Regression[a] Predicting Receipt of Primary Tumor Therapy and Systemic Adjuvant Therapy[b,c]

	No/Yes	Yes/No	Yes/Yes
Characteristics	OR[a] (95% CI)	OR[a] (95% CI)	OR[a] (95% CI)
Surgeon Gender			
Female	3.1 (1.8, 5.5)	2.7 (1.6, 4.7)	4.5 (2.7, 7.7)
Male	— 1.0 —	— 1.0 —	— 1.0 —

[a] Receipt of neither therapy (no/no) is the referent group

[b] Adjusted for age, stage, education, and marital status

[c] No/Yes = No definitive primary tumor therapy

Systemic adjuvant therapy

Yes/No = Definitive primary tumor therapy

No systemic adjuvant therapy

Yes/Yes = Definitive primary tumor therapy

Systemic adjuvant therapy

Patient Characteristics and Treatments Associated with a Decline in Upper-body Function Following Breast Cancer Therapy

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ABSTRACT

Patient characteristics and treatments associated with a decline in upper-body function following breast cancer therapy

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Breast cancer therapy is often followed by a decline in upper-body function. 303 women diagnosed with Stage I or II breast cancer were interviewed 5 and 21 months after surgery and their medical records were reviewed. Women with cardiopulmonary comorbidity had an odds ratio for decline at the 5 month interview of 2.8 (95 percent CI 1.3-5.7), relative to women without. Women who received mastectomy (OR = 2.5; 95 percent CI 0.9-6.7) or breast conserving surgery with radiation therapy (OR = 2.9; 95 percent CI 1.0-8.9) were at higher risk for decline at the 5 month interview than women who received only breast conserving surgery. Women who had axillary dissection were more likely to report numbness or pain in the axilla (OR = 6.4; 95 percent CI 1.2-33) at the 21 month interview than women who did not. Clinicians should consider the functional consequences of treatment when discussing treatment options and post-operative care with women who have early stage breast cancer.

Key Words: breast neoplasms, complications; breast neoplasms, therapy

Running title: Upper-body function decline following breast cancer

INTRODUCTION

Breast cancer is an important cause of morbidity and mortality among women. The American Cancer Society estimated that 178,700 women were diagnosed with breast cancer in 1998 and that 43,500 women died from the disease [1]. The large number of breast cancer cases diagnosed each year, in combination with the relatively favorable survival rates for treated patients, yields the largest group of cancer survivors in the U.S. population. Nearly two million living U.S. women have been diagnosed with breast cancer [2]. This sizeable pool of prevalent survivors suggests that the quality of life after breast cancer therapy is an important issue [3]. Quality of life strongly depends on physical function, both of which decline on average following breast cancer therapy [4].

While it is reasonable to expect that patients' upper-body function will decline following breast cancer therapy, studies have only recently characterized the nature, determinants, and duration of impairment [3-6]. An accurate understanding of the patient characteristics and therapy options that predispose towards upper-body dysfunction and discomfort is essential. Such an understanding would allow physicians to include consideration of the potential for these sequelae in their treatment recommendations and to prescribe exercise interventions that can be initiated before surgery.

This study assessed the effect of patient characteristics and therapy on self-reported upper-body function and discomfort 5 months after and 21 months after primary breast cancer therapy. The study provides some guidance as to the identification of patients likely to suffer upper-body sequelae and the treatments that may induce these adverse effects.

METHODS

Sampling

Details of the study have been described elsewhere [7]. An initial analysis of the effects of patient characteristics and therapy on upper-body function three to five months after definitive surgery has been presented [8]. The focus of the earlier presentation was to develop a parsimonious model to predict upper-body function decline. This presentation shows mutually adjusted effects of all patient characteristics and therapies, is not limited to a subset of respondents, and investigates effects at the first follow-up interview as well as at the baseline interview.

We studied women ≥ 55 years of age, newly diagnosed with histologically confirmed stage I or stage II invasive breast carcinoma, and treated at one of 5 hospitals in Boston, Massachusetts. We sent an introductory letter and a consent form to 388 potential study participants whose surgeons permitted contact. The letters were sent two to three months after the

patient's definitive surgical treatment. An interviewer followed-up with a telephone call to explain the study further, to answer questions, and to obtain informed consent. The average time from definitive surgery to baseline interview was 136 days (range 66 days to 293 days). We completed 90 percent of the baseline interviews by 185 days after definitive surgery. We attempted to contact all women for a follow-up interview. The average time from definitive surgery to the follow-up interview was 623 days, with a minimum of 473 days and a maximum of 1092 days. We completed 90 percent of the follow-up interviews by 693 days after definitive surgery.

Data collection

We reviewed patients' surgical records and conducted two 35-minute computer-assisted telephone interviews with consenting eligible patients. Data collected from medical records included: tumor size, axillary node status, breast surgery or surgeries performed (mastectomy or breast conserving surgery, with or without axillary dissection), side of surgery, and whether or not the patient received a course of post-operative radiation therapy.

Both the baseline and follow-up telephone interviews included three questions about tasks that required upper-body function: 1) pushing or pulling large objects, such as a living room chair, 2) lifting objects weighing more than 10 pounds, such

as a heavy bag of groceries, and 3) reaching or extending arms above shoulder level. We asked subjects to characterize the difficulty of each task as very difficult, somewhat difficult, or not difficult – or to say they did not do the task – during the four weeks preceding the interviews. We also asked subjects to characterize the difficulty of the tasks prior to their breast cancer treatment. We assumed that subjects who said they did not do a task had the most difficulty with that task, although we recognize that subjects might not do a task for reasons other than difficulty performing it. When we assumed that subjects who said they did not do a task had the least difficulty with that task, the results presented herein did not change substantially.

We selected these tasks to measure upper-body function from the items used by Satariano and colleagues [3], fielded previously in the Framingham Disability Study [9] and originally developed by Nagi [10].

We also asked subjects at the follow-up interview whether they were bothered by numbness or pain in their axilla as a result of surgery and whether they were bothered by swelling or problems with their arm as a result of surgery.

To characterize potential covariates, we asked questions about cardiopulmonary comorbidities that were part of the Total Illness Burden Index [11] and about patients' age, race, marital

status, education, number of people in the household, height, and weight.

Major analytic variables

Our primary dependent variable was a decline in upper-body function. Patients were classified as having an early decline in upper-body function for any task if they responded that any of the three tasks was more difficult at baseline interview than it was before breast cancer treatment. Patients were classified as having a late decline in upper-body function for any task if (1) they responded that any of the three tasks was more difficult at baseline interview than it was before breast cancer treatment and they did not recover to at least the baseline level of difficulty by the follow-up interview, or (2) they responded that any of the three tasks was more difficult at the follow-up interview than it was at the baseline interview.

Secondary dependent variables included two characterizations of upper-body discomfort. The first was a self-report at the follow-up interview of numbness or pain in the axilla as a result of surgery. The second was a self-report at the follow-up interview of swelling or problems with an arm as a result of surgery.

For our independent variables we considered: age (categories of 55-64, 65-74, 75+); education (< high school or ≥ high school); number of residents in the household (lives alone or

lives with somebody else); and marital status (married or other). We also considered body mass index (categorized as <25 kg/m^2, ≥ 25 to <30 kg/m^2, or ≥ 30 kg/m^2 [12]); tumor stage (stage I or stage II); side of surgery (categorized as right or both sides versus left side); breast cancer treatments received, cardiopulmonary comorbidity [13] (categorized as a score of 0, 1 to 3, or 4 or more – based on patients' reports of diagnoses of chronic obstructive pulmonary disease, congestive heart failure, and ischemic heart disease or related symptoms of severity – with a higher score reflecting a diagnosis of at least one of the diseases or severe symptoms of the diseases without a formal diagnosis). A cardiopulmonary comorbidity score of 4 might reflect, for example, diagnoses of both heart attack and angina; or diagnosis of emphysema, chronic bronchitis or asthma; or diagnosis of congestive heart failure.

For the breast cancer treatments variables, we considered three primary treatments (breast conserving surgery followed by radiation therapy or simple mastectomy, versus receipt of breast conserving surgery with no radiation therapy) and whether or not subjects had axillary dissection.

Analytic Strategy

We performed a series of bivariate analyses, examining the relationships between independent variables and the dependent variables. Next, we developed a multiple logistic regression

model for each outcome: early decline in upper-body function, late decline in upper-body function, and each measure of upper-body discomfort. Because of the range of times between definitive surgery and the interviews, we included days between definitive surgery and the interviews in the applicable multivariable regression models. We did not perform survival analyses because the time to decline was determined by the date of interview, so does not correspond to the true time to the event.

RESULTS

We interviewed 303 women at the baseline interview following their definitive surgery. The 303 patients represent 78% of the 388 women whose surgeon permitted contact. Two hundred and fifty of the 303 women then completed the follow-up interview. Of the 53 women lost to follow-up, 5 died, 16 refused to participate in the follow-up interview, 2 were unable to participate because of poor health, and 30 could not be contacted. The women lost to follow-up were older, less likely to be married, and had lower body mass index, though these differences were not substantial. The risk of upper-body function decline did not depend on time to baseline or follow-up interview.

Table 1 shows the characteristics of the 303 women who completed the baseline interview. Of these women, 58% were $\geq$ 65 years of age. Most were white (93%) and had a high school

education or greater (83%). Half were married; most of the remainder were widowed. The average body mass index was 26.0 ± 0.3 kg/m^2 and the average comorbidity score was 1.5 ± 0.1. Most patients had small tumors (77% ≤ 2 cm) and were node negative (80%). The majority (65%) had undergone breast conserving surgery followed by radiation therapy; 24% had undergone mastectomy. Almost all (85%) had undergone axillary dissection.

At the baseline interview, 36% of subjects reported some decline in upper-body function and 7% reported a decline in all three of the upper-body function tasks. At the follow-up interview, 36% of subjects reported some decline in upper-body function and 4% reported a decline in all three of the upper-body function tasks. Two-thirds of the women who reported some decline in upper-body function at follow-up interview also reported a decline in upper-body function at the baseline interview.

The only patient characteristics associated with any early decline in upper-body function were cardiopulmonary comorbidity and education (see Table 2 for measures of the effect of patient characteristics on upper-body function decline). Women with a cardiopulmonary comorbidity score of 1, 2, or 3 had an odds ratio for any early upper-body function decline of 1.3 (95 percent CI 0.7-2.4), relative to women with a score of 0. Women with a cardiopulmonary comorbidity score of 4 or more had an odds ratio

for any early upper-body function decline of 2.8 (95 percent CI 1.3-5.7), relative to women with a score of 0. The latter association was attenuated for some late decline in upper-body function. Women with a cardiopulmonary comorbidity score of 1, 2, or 3 had an odds ratio for any late upper-body function decline of 1.2 (95 percent CI 0.6-2.4), relative to women with a score of 0. Women with a cardiopulmonary comorbidity score of 4 or more had an odds ratio for any late upper-body function decline of 1.7 (95 percent CI 0.8-3.8), relative to women with a score of 0. Women with at least a high school education were at lower risk for upper-body function decline at the 21 month interview (OR = 0.4; 95 percent CI 0.2-1.0).

Women who received mastectomy (OR = 2.5; 95 percent CI 0.9-6.7) or breast conserving surgery with radiation therapy (OR = 2.9; 95 percent CI 1.0-8.9) were at higher risk for upper-body function decline at the 5 month interview than women who received only breast conserving surgery.

At the follow-up interview, 37% of women reported numbness or pain in the axilla and 17% reported swelling or other problems with an arm. Older women were less likely than younger women to report numbness or pain in the axilla (see Table 3 for measures of the effect of patient characteristics on upper-body discomfort). In addition, women who lived alone were more likely

to have swelling or other arm problems than women who did not live alone (OR = 4.1; 95 percent CI 1.2-14).

Although the effect of axillary dissection on decline in upper-body function did not persist to the follow-up interview, axillary dissection did affect upper-body discomfort at the follow-up interview (see Table 3 for measures of the effect of patient characteristics on upper-body discomfort). Women who had axillary dissection were more likely to report numbness or pain in the axilla (OR = 6.4; 95 percent CI 1.2-33) than women who did not have axillary dissection.

DISCUSSION

As reported previously [8], breast cancer patients with cardiopulmonary comorbidity or who received definitive primary therapy (breast conserving surgery and radiation therapy, or mastectomy) are at increased risk of decline in upper-body function during the five months following primary breast cancer therapy. Age, marital status, living alone, and side of surgery were not related to decline in upper-body function in either the 5 months following definitive surgery or at the 21-month follow-up.

Axillary dissection was an important cause of upper-body discomfort at the follow-up interview 21 months after definitive surgery. Approximately 40% of women who had axillary dissection reported pain in their axilla at the follow-up interview,

compared to 7% of those who did not have axillary dissection. Approximately 20% of women who had axillary dissection reported swelling or other arm problems at the follow-up interview, compared to 3% of women who did not have axillary dissection. Younger women were more likely than older women to report upper-body discomfort and women who lived alone were more likely to report swelling or other arm problems than women who did not live alone. Marital status, education, side of surgery, and cardiopulmonary comorbidity were not related to upper-body discomfort at the follow-up interview.

Axillary node dissection may increase the risk of decline in upper-body function in the 5 months after treatment, but not the risk of persistent decline or delayed onset of decline 21 months after definitive surgery. As expected, axillary dissection appears to increase the risk of numbness or pain in the axilla, even two years after diagnosis.

Our findings are consistent with previous investigations of upper-body function after treatment for early stage breast cancer. Liljegren and colleagues found that older patients and patients who underwent less extensive axillary dissection were at lower risk for arm symptoms at both 3-12 months and 13-36 months after treatment [14]. Three other investigations also found that the prevalence of upper-body sequelae depended on the extent of axillary dissection [15, 16, 17]. Ganz and colleagues found that

measures of quality life after treatment did not depend on receipt of breast conserving surgery versus modified radical mastectomy, except that patients who received the latter primary therapy were more likely to report problems with clothing and body image [18]. Tasmuth and colleagues found that the occurrence of arm sequelae did not depend on whether the patient received breast conserving surgery or modified radical mastectomy and that reaching out, carrying heavy objects, working with the ipsilateral arm, and housework aggravated the arm symptoms [19]. These aggravating factors may be among the influences captured in our finding that women who live alone were more likely to report swelling or other arm problems.

Gerber and colleagues found that women who received modified radical mastectomy recovered their pre-operative range of motion more slowly than women who received local excision and radiation therapy [5]. The difference in recovery time for functional range of motion was not as large as the difference in recovery time for pre-operative range of motion. Sneeuw and colleagues examined functional outcomes four years after treatment among women who received breast conserving surgery, axillary dissection, and radiation therapy [6]. Nearly half of the subjects reported a little (34%) or moderate (13%) limitation of movement in the arm and shoulder on the treatment side.

Axillary node dissection is an important prognostic indicator for women with early stage breast cancer [20]. Removal of level 1 and level 2 nodes is currently recommended for accurate staging and to reduce the risk of recurrence in the axilla, unless the risk of axillary metastasis is very low or when knowledge of node status will have no influence on therapy [21]. Reliable indicators of node status to stage disease accurately when no axillary dissection is performed, however, have been difficult to identify [22].

Although there is a general consensus regarding the current need for axillary dissection to facilitate staging and to avoid axillary metastasis, the extent of dissection remains controversial [21]. Axillary sampling of 3 to 5 nodes, which had shown some promise [23], has largely been abandoned in favor of dissection of only level I and level II nodes [21, 24, 25]. Levels I and II dissection yields 10 or more nodes, which is usually sufficient to determine the breast cancer stage [21]. The advent of lymphatic mapping and sentinel lymph node biopsy may further reduce the extent of recommended axillary dissection [26]. In three recent series of clinically node-negative breast cancer patients, sentinel lymph node biopsy detected between 89% and 98% of patients with positive nodes by level I-III axillary dissection and all patients with negative nodes by level I-III axillary dissection had a negative sentinel lymph node biopsy

[27, 28, 29]. While these results suggest that sentinel node biopsy may eventually supplant axillary dissection for breast cancer staging, current recommendations conclude that it would be premature to abandon axillary dissection in favor of sentinel node biopsy [30] without clinical trials to establish its safety and efficacy [31]. Furthermore, axillary dissection will remain an important component of prognostic evaluation for women whose sentinel node biopsy results are positive.

Our findings must be considered with the study's major limitations in mind. First, we did not directly measure upper-body function, either before or after treatment. We asked women to recall their upper-body function prior to their treatment, and then compared their current self-reported function to the prediagnosis function as a measure of upper-body function decline. While this method may misclassify decline in upper-body function, we do not expect the misclassification to depend on cardiopulmonary comorbidity status or primary therapy. Non-differential misclassification of upper-body function would bias the estimated effect of cardiopulmonary comorbidity towards the null on average. Differential recall is more likely associated with axillary dissection, a surgical intervention that women may expect will cause a decline in upper-body function. We would not, however, expect this differential recall to dissipate by the 21-month time point, and axillary dissection was only associated

with upper-body function decline between the prediagnosis assessment and the 5 month time point. In addition, the score of self-reported prediagnosis upper-body function summed over the three tasks did not depend on any of the patient or therapy characteristics (2-sided null p-value for the association with breast conserving surgery and radiation therapy = 0.79, with mastectomy = 0.76, and with axillary dissection = 0.82) except the cardiopulmonary comorbidity index (2-sided null p-value = 0.0004), which reflects the impact of diseases that existed at the time of the first interview. These findings suggest that the self-reported assessment of prediagnosis upper-body function was not biased by the therapy that the participants received. We conclude that differential misclassification is unlikely to account for the entire association between cardiopulmonary comorbidity, primary therapy, or axillary dissection, and upper-body function decline.

Furthermore, some earlier investigators have argued that patient's self-report of arm function is likely to be more relevant than objective measures [32, 33, 34]. These investigators contend that objective measures of function do not adequately reflect patients' perceptions of their function and ability to perform activities of daily living. Patients with poor objective measures may report no impact on their upper-body

function and patients with poor self-reported function may score in the normal range of objective measures.

Second, we did not gather side of surgery information in relation to handedness. One earlier investigation showed that grip strength declined more if surgery was performed on the side of the dominant hand [19]. As a crude approximation, we measured the effect of side of surgery on the upper-body outcomes. If one assumes that all women in the cohort are right handed, then side of surgery crudely approximates the effect of surgery on the side of a woman's dominant hand. Approximately 6% of women in the study's age range are expected to be left handed [35], so would be misclassified as right handed in this analysis. Side of surgery had no effect on upper-body function decline or discomfort. If surgery on the side of the dominant hand is more likely to result in upper-body function decline than surgery on the side of the less dominant hand, we would have expected to see some effect. It may be that the measures of upper-body function decline are too crude to detect a hand-dependent effect. Measures of fine motor control or sensation, for example, may be more dependent on whether surgery occurs on the side of the dominant hand.

Third, we did not collect information about prior recreational or occupational injuries involving the upper extremities. We do not expect these to depend on the variables

included in the analysis, so the reported measures of effect should not be confounded by these prior conditions.

Fourth, we did not measure upper-body function decline in a control population that was not diagnosed with breast cancer. Thus, we cannot measure the effect of the diagnosis and/or receipt of any primary therapy on upper-body function and discomfort. Satariano and Ragland [36] measured the prevalence of upper-body function limitation in both a control population and a population of breast cancer patients. They defined a limitation as any report of a lot of difficulty, or that the task was not performed on doctor's orders, for any of the upper-body tasks originally developed by Nagi [10]. Using a similar definition for upper-body limitation at baseline interview, and stratifying our population into the age groups used by Satariano and Ragland [36], we found that the prevalence of upper-body limitation in our population of breast cancer patients more closely resembled the prevalence of upper-body limitation in the control population of Satariano and Ragland [36] than the prevalence in their population of breast cancer patients (data not shown). Satariano and Ragland asked subjects about limitations in lifting items that weigh less than ten pounds, and we did not. The difference in prevalence of upper-body limitation between our breast cancer patients and their breast

cancer patients may be partly explained by their inquiry about this additional task.

Given the critical importance of upper-body function in maintaining independent living [37], our findings suggest that clinicians should consider the functional consequences of treatment when discussing treatment options and post-operative care with older women who have early stage breast cancer. Strategies to prevent overcompensation for discomfort or weakness on the side of surgery by overusing the opposite side should also be outlined.

This study demonstrates that upper-body dysfunction can arise shortly after therapy and resolve, arise and persist for at least 21 months, or arise at some time distant from therapy. Therefore, the upper-body function of all breast cancer patients should be followed and appropriate interventions planned for at least two years after diagnosis. In time, surgeons and patients may be able to substitute sentinel node biopsy for axillary dissection to reduce the impact of breast cancer therapy on upper body function.

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Table 1. Characteristics of the cohort

Characteristic	Number	Percent
Age group		
55-64 years	126	42%
65-74 years	111	37%
75+ years	66	22%
Race		
White	281	93%
African American	13	4%
Hispanic	2	0.7%
Asian or Pacific Islander	3	1%
Other	2	0.7%
Missing	2	
Education		
< High School	51	17%
≥ High School	249	83%
Missing	3	
Number in House		
Lives with someone	197	66%
Lives alone	103	34%
Missing	3	

Characteristic	Number	Percent
Marital Status		
Other than married	153	51%
Married	148	49%
Missing	7	
Body Mass Index		
<25 kg/m2	143	48%
≥25 to <30 kg/m2	100	34%
≥30 kg/m2	55	19%
Missing	5	
Tumor Stage		
Stage 1	193	64%
Stage 2	109	36%
Missing	1	
Side of Surgery		
Left Only	123	49%
Right or Both	126	51%
Missing	54	

Characteristic	Number	Percent
Cardiopulmonary Comorbidity Score		
Zero	180	59%
One, two or three	73	24%
Four to fifteen	50	17%
Primary therapy		
Mastectomy	71	23%
Breast conserving surgery and radiation therapy	195	64%
Breast conserving surgery and no radiation therapy	33	11%
Other	4	1%
Axillary Dissection		
No	44	15%
Yes	258	85%
Missing	1	

Table 2. Effect of patient characteristics and therapy on early and late upper-body function

	Decline from baseline to 5 month interview			Decline from baseline to 21 month interview		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Age group						
55-64 years	45/126	36%	1.	36/107	34%	1.
65-74 years	40/110	36%	0.9 (0.5-1.7)	32/95	34%	0.8 (0.4-1.5)
75+ years	21/62	34%	1.2 (0.5-2.7)	23/48	48%	1.1 (0.4-2.6)
Missing	5			7		

	Decline from baseline to 5 month interview			Decline from baseline to 21 month interview		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Race†						
White	100/276	36%		84/237	35%	
African American	5/13	38%		4/9	44%	
Hispanic	1/2	50%		1/1	100%	
Asian or Pacific Islander	0/2	0%		1/2	50%	
Other	0/2	0%				
Missing	7			2		

	Decline from baseline to 5 month interview			Decline from baseline to 21 month interview		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Education						
< High School	30/50	40%	1.	22/40	55%	1.
≥ High School	86/246	35%	0.9 (0.4-1.7)	68/209	33%	0.4 (0.2-1.0)
Missing	7			2		
Number in House						
Lives with someone	67/194	35%	1.	50/164	30%	1.
Lives alone	38/101	38%	1.0 (0.5-2.2)	39/84	46%	1.5 (0.7-3.5)
Missing	8			3		

	Decline from baseline to 5 month interview			Decline from baseline to 21 month interview		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Marital Status						
Other than married	58/148	39%	1.	55/121	45%	1.
Married	48/148	32%	0.8 (0.4-1.6)	35/128	35%	0.7 (0.3-1.6)
Missing	7			2		
Body Mass Index						
<25 kg/m2	46/141	33%	1.	44/116	38%	1.
≥25 to <30 kg/m2	34/99	34%	1.0 (0.6-1.8)	26/84	31%	0.6 (0.3-1.3)
≥30 kg/m2	26/55	47%	1.5 (0.7-3.1)	20/48	42%	1.0 (0.5-2.3)
Missing	8			3		

	Decline from baseline to 5 month interview			Decline from baseline to 21 month interview		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Tumor Stage						
Stage 1	65/188	35%	1.	61/163	37%	1.
Stage 2	41/109	38%	1.0 (0.5-1.7)	30/87	34%	0.9 (0.5-1.7)
Missing	6			1		
Side of Surgery‡						
Left Only	42/123	34%	1.	45/120	38%	1.
Right or Both	46/125	37%	1.2 (0.7-2.0)	41/124	33%	0.8 (0.5-1.4)
Missing	55			7		

	Decline from baseline to 5 month interview			Decline from baseline to 21 month interview		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Cardiopulmonary Comorbidity Score						
Zero	53/177	30%	1.	46/145	68%	1.
One, two or three	27/72	38%	1.3 (0.7-2.4)	23/62	63%	1.2 (0.6-2.4)
Four to fifteen	26/49	53%	2.8 (1.3-5.7)	22/43	49%	1.7 (0.8-3.8)
Missing	5			1		

	Decline from baseline to 5 month interview			Decline from baseline to 21 month interview		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Primary therapy						
Mastectomy	30/69	43%	2.5 (0.9-6.7)	21/55	38%	1.3 (0.5-3.6)
Breast conserving surgery and radiation therapy	69/194	36%	2.9 (1.0-8.9)	59/168	35%	1.3 (0.4-4.3)
Breast conserving surgery and no radiation therapy	6/31	20%	1.	11/27	41%	1.
Other	9			1		

	Decline from baseline to 5 month interview			Decline from baseline to 21 month interview		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Axillary Dissection						
No	10/40	25%	1.	15/30	50%	1.
Yes	95/257	95/2	2.5 (0.9-6.6)	75/219	34%	0.8 (0.3-2.2)
Missing	6	57		2		

*Unless otherwise indicated, adjusted for the effects of the other listed variables, time to baseline interview, and time to follow-up interview (for dependent variables measured at the follow-up).

†Race was not included in the multivariable models because of the small number of nonwhite subjects.

‡The effect of side of surgery was adjusted for the other variables. Side of surgery was not included in the multivariable models to estimate the effects of the other variables because of the high proportion of subjects for whom side of surgery was unknown.

Table 3. Effect of patient characteristics on numbness, pain or swelling at follow-up interview

	Numbness or pain in the axilla			Swelling in the arm		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Age group						
55-64 years	60/105	57%	1.	19/105	18%	1.
65-74 years	26/93	28%	0.2 (0.1-0.5)	19/94	20%	1.2 (0.5-2.7)
75+ years	6/48	13%	0.1 (0.03-0.3)	4/48	8%	0.3 (0.1-1.3)
Missing	5			4		

	Numbness or pain in the axilla			Swelling in the arm		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Race†						
White	85/234	36%		39/235	17%	
African American	5/8	63%		2/8	25%	
Hispanic	0/1	0%		0/1	0%	
Asian or Pacific Islander	1/2	50%		1/2	50%	
Other	7					
Missing				5		

	Numbness or pain in the axilla			Swelling in the arm		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Education						
< High School	14/40	35%	1.	8/40	20%	1.
≥ High School	77/205	38%	0.5 (0.2-1.2)	34/206	17%	0.8 (0.3-2.2)
Missing	7			5		
Number in House						
Lives with someone	65/161	40%	1.	25/162	15%	1.
Lives alone	26/83	31%	1.5 (0.6-3.6)	17/83	20%	4.1 (1.2-14)
Missing	8			6		

	Numbness or pain in the axilla			Swelling in the arm		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Marital Status						
Other than married	39/119	33%	1.	20/119	17%	1.
Married	52/126	41%	1.2 (0.5-2.7)	22/127	17%	2.3 (0.7-7.1)
Missing	7			5		
Body Mass Index						
< 25 kg/m2	43/113	38%	1.	15/114	13%	1.
≥25 to <30 kg/m2	27/83	33%	0.6 (0.3-1.3)	14/83	17%	1.0 (0.4-2.5)
≥30 kg/m2	21/48	44%	0.7 (0.3-1.6)	13/48	27%	2.4 (0.9-6.7)
Missing	8			6		

	Numbness or pain in the axilla			Swelling in the arm		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Tumor Stage						
Stage 1	58/160	36%	1.	21/161	13%	1.
Stage 2	34/86	40%	0.9 (0.5-1.7)	21/86	24%	2.0 (0.9-4.3)
Missing	6			4		
Side of Surgery						
Left Only	45/119	38%	1.	24/120	20%	1.
Right or Both	46/125	37%	1.1 (0.6-1.9)	18/125	14%	0.6 (0.3-1.2)
Missing	8			6		

	Numbness or pain in the axilla			Swelling in the arm		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Cardiopulmonary Comorbidity Score						
Zero	54/142	38%	1.	26/143	18%	1.
One, two or three	22/61	36%	1.3 (0.6–2.8)	10/61	16%	0.7 (0.3–1.7)
Four to fifteen	16/43	37%	1.9 (0.8–4.5)	6/43	14%	0.6 (0.3–1.7)
Missing	3			4		

	Numbness or pain in the axilla			Swelling in the arm		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Primary therapy						
Mastectomy	19/53	36%	1.6 (0.4-6.2)	13/53	25%	2.5 (0.5-13)
Breast conserving surgery and radiation therapy	66/166	40%	2.2 (0.6-7.5)	26/167	16%	1.5 (0.3-7.0)
Breast conserving surgery and no radiation therapy	5/25	20%	1.	3/25	11%	1.
Other	4			4		

	Numbness or pain in the axilla			Swelling in the arm		
	# declining/ total	% Declining	adjusted* OR (95% CI)	# declining/ total	% Declining	adjusted* OR (95% CI)
Axillary Dissection						
No	2/30	7%	1.	1/30	3%	1.
Yes	90/216	42%	6.4 (1.2-33)	41/217	19%	3.8 (0.4-34)
Missing	6			4		

*Unless otherwise indicated, adjusted for the effects of the other listed variables and time to follow-up interview.

†Race was not included in the multivariable models because of the small number of nonwhite subjects.

DEPARTMENT OF THE ARMY
US ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
504 SCOTT STREET
FORT DETRICK, MARYLAND 21702-5012

REPLY TO
ATTENTION OF:

MCMR-RMI-S (70-1y) 23 Aug 01

MEMORANDUM FOR Administrator, Defense Technical Information Center (DTIC-OCA), 8725 John J. Kingman Road, Fort Belvoir, VA 22060-6218

SUBJECT: Request Change in Distribution Statement

1. The U.S. Army Medical Research and Materiel Command has reexamined the need for the limitation assigned to the technical reports listed at enclosure. Request the limited distribution statement for these reports be changed to "Approved for public release; distribution unlimited." These reports should be released to the National Technical Information Service.

2. Point of contact for this request is Ms. Judy Pawlus at DSN 343-7322 or by e-mail at judy.pawlus@det.amedd.army.mil.

FOR THE COMMANDER:

Phylis Rinehart

Encl

PHYLIS M. RINEHART
Deputy Chief of Staff for
Information Management

Reports to be Downgraded to Unlimited Distribution

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